# American Journal of

### OBSTETRICS AND GYNECOLOGY

### Obstetrics

#### ANTEPARTUM HEMORRHAGE\*

to M. se

ie

rd

n-

al

A Review of 383 Cases of Abruptio Placentae and 169 Cases of Placenta Previa Treated During the Years 1944 to 1957

ROBERT A. KIMBROUGH, M.D., PHILADELPHIA, PA.

(From the Philadelphia Lying-In Division of the Pennsylvania Hospital)

THE management of hemorrhage during the last trimester of pregnancy constitutes one of our most important and controversial obstetrical problems. This presentation consists of a review of 552 such instances occurring in the Philadelphia Lying-In Division of the Pennsylvania Hospital.

#### Part I. Abruptio Placentae

During the 14 year period from 1944 through 1957 there were 41,919 deliveries; among these, 383 patients had premature separation of the normally situated placenta after the twenty-eighth week of pregnancy, representing an incidence of one such complication in 109 deliveries (Table I). This period of time was chosen as it more clearly represents our current management than would a study extending further into the past.

TABLE I. INCIDENCE OF PREMATURE SEPARATION OF THE PLACENTA

Total No. of deliveries	41,919
No. of cases of abruptio placentae	383
Incidence of abruptio placentae	1 in 109

This study is based upon cases in which there was clinical evidence of separation; minor degrees of separation which were discovered only after

<sup>\*</sup>Presented as the Ninth Annual Joseph L. Baer Lecture before the Chicago Gynecological Society, Oct. 17, 1958.

delivery of the placenta by the presence of minute retroplacental clots or small organized areas of separated placental tissue have not been included.

TABLE II. ETIOLOGICAL FACTORS IN PREMATURE SEPARATION

	NO.	%
Toxemia of late pregnancy	33	8.8
Unknown	350	91.2
Total	383	100

While hypertensive toxemia of pregnancy and hypertensive cardiovascular disease were found in only 8.8 per cent of our patients (Table II), in many of those in whom there was no elevation of blood pressure or proteinuria, abnormal gain in weight and edema strongly suggested the presence of toxemia. A pre-existing hypertension in others may have been masked by a fall in blood pressure incident to hemorrhage. Dieckmann, in contrast, found that 69 per cent of his patients with abruptio placentae had evidence of toxemia. Hertig, too, holds that toxic separation of the placenta is a form of "uterine eclampsia" since fatal cases have hepatic lesions which are not distinguishable from those of ordinary eclampsia.

Direct trauma to the uterus as from a blow on the abdomen may produce retroplacental hemorrhage. Indirect trauma from a sudden jar, coitus, or even severe coughing also may produce this complication. Among our patients, trauma was possibly responsible in only one instance, this having been a kick in the abdomen.

#### Symptomatology

The constitutional symptoms of the mother usually were in direct proportion to the amount of hemorrhage. The cases of severe hemorrhage most often occurred before the onset of labor and the bleeding was more frequently concealed for a comparatively long period. The mild cases occurred usually in the course of labor and in these the bleeding was largely external.

Fibrinogenopenia is associated with abruptio placentae in a sufficient number of cases to require determination of the level of fibrinogen in each suspicious case. Presumably, absorption of thromboplastin from the retroplacental area produces first intravascular coagulation of fibrin and later a critical fall in available fibrinogen; this results in absence or deficiency of clot formation. Weiner, Reid, and Roby<sup>3</sup> have stated that rupture of the membranes, reducing intracavitary pressure, often will reduce the absorption of thromboplastin; this mechanism, however, cannot be anticipated with certainty. Prompt replacement of fibrinogen in pure form is imperative if the level is found to be low.

Fibrinogenopenia of sufficient degree to be of clinical importance was found in only 4 of our patients during the past 5 years. Three of these were delivered spontaneously and one required cesarean section. Three of the 4 mothers recovered; the other died, presumably of amniotic fluid embolism. Three of the babies died in utero as a result of massive placental separation. Fibrinogen was administered to each patient after it was determined that a deficient level existed.

In addition to excessive bleeding during labor, one of these patients presented a bizarre neurological picture which was thought to be due to cerebral lodgement of fibrin emboli incident to intravascular clotting. She recovered completely within 48 hours after delivery.

Fortunately, three-fifths of the separations occurred during labor and did not, therefore, constitute the greatest hazard (Table III).

n e y

a

r

TABLE III. TIME OF OCCURRENCE OF ABRUPTIO PLACENTAE

	CASES	%
Before labor	157	41.0
During labor	226	59.0
Total	383	100.0

The mild cases were those occurring, almost without exception, during labor, and they were manifested by somewhat more than usual bleeding, some increase in uterine tension, and, occasionally, evidence of slight or moderate fetal distress. The severe instances were those in which there was evidence of a large concealed or frank external hemorrhage (Table IV).

TABLE IV. SEVERITY OF CASES OF ABRUPTIO PLACENTAE

Mild	199	
Moderate	199 100	
Severe	84	
Total	383	

#### Management

Our choice of management is dependent upon the severity of the symptoms, the presence or absence of good clot formation, the condition of the fetus, whether or not the patient is in labor, and, most important of all, the degree of cervical effacement and dilatation.

In those instances in which the separation occurred in the course of labor, the condition of the mother and fetus usually remained satisfactory. Most often little more was necessary than the administration of oxygen and increased caution on the part of the obstetrician.

As seen in Table V, more than two-thirds of our patients were delivered vaginally.

TABLE V. METHOD OF DELIVERY IN CASES OF ABRUPTIO PLACENTAE

	CASES	%
Vaginal delivery Forceps Spontaneous Podalic version Breech extraction	269 177 68 1 23	70.2
Abdominal delivery Cesarean section Porro cesarean	113 1	29.8
Total No. of cases	383	100.0

In the more severe examples, particularly those in which the separation occurs before the onset of labor, cesarean section is more often our method of delivery. Not until the uterus is empty can firm contraction of the uterus close the bleeding sinuses at the placental site. Among 222 patients in whom placental separation occurred during labor, more than 90 per cent were delivered vaginally. Of the 161 instances occurring before the onset of labor, three-fifths were managed by cesarean section (Table VI).

In the more urgent cases, cesarean section occasionally is done in the interest of the mother even though the child is known to be dead. Before

instituting any procedure for delivery, the patient must be treated for shock, and lost blood must be replaced. While the necessary preparations for cesarean section are awaited, the membranes are ruptured to decrease absorption of thromboplastin and to hasten labor. Under these circumstances rapid dilatation of the cervix often obviates the need for cesarean section. If there is a disturbance of the clotting mechanism, fibrinogen must be administered in adequate amounts. A fine point of judgment is required in determining how long to postpone operative measures while reaction from shock is awaited. No arbitrary rules can be stated since each patient must be considered according to prevailing circumstances.

TABLE VI. METHOD OF DELIVERY ACCORDING TO TIME OF ONSET OF SYMPTOMS AS RELATED TO LABOR

	CASES	%
Abruptio placentae during labor	222	
Cesarean section	17	7.7
Vaginal delivery	205	92.3
Abruptio placentae before labor	161	
Cesarean section	97	60.2
Vaginal delivery	64	39.8

Removal of the uterus was deemed advisable for only one of the patients who were managed by cesarean section. We do not remove the uterus simply because of its darkened and contused appearance from extravasation of blood, but only if it fails to contract after its evacuation.

Following delivery precaution must be taken against postpartum hemorrhage. Many of these uteri fail to remain firmly contracted and a small amount of additional bleeding will be tolerated poorly by the patient who already has suffered a considerable loss of blood. The administration of oxytocin in dilute solution intravenously following delivery has lessened the incidence of hemorrhage.

### Maternal Mortality

The patient who died (Tables VII and VIII) was a gravida i, para o, at term. She was admitted with an excessive bloody show, in labor, and there was some undue tenderness of the uterus. A presumptive diagnosis of partial premature separation of the placenta was made. The membranes were ruptured artificially and good labor ensued. There was no further bleeding or evidence of fetal distress. The patient was delivered easily of a living male infant after 3 hours of labor. Following delivery, although the uterus was firmly contracted, bleeding continued. The uterine cavity was explored

TABLE VII. MATERNAL MORTALITY FROM ABRUPTIO PLACENTAE

	NO.	%
No. of cases of abruptio placentae	383	
No. of maternal deaths from abruptio placentae	1	0.26

TABLE VIII. MATERNAL MORTALITY ACCORDING TO METHOD OF DELIVERY

	DEATHS	CASES	%
Vaginal delivery	1	269	0.36
Cesarean section	0	114	0.00
Total maternal mortality	1	383	0.2

9

7

and neither tear nor placental tissue was found. The blood failed to coagulate; whole blood and 1 Gm. of fibrinogen were given. A total hysterectomy was performed. As the procedure was being completed the patient stopped breathing; despite cardiac massage, she died. Necropsy was not permitted. The uterine veins were filled with amniotic fluid. The cause of death was thought to be amniotic fluid embolism.

#### Fetal Mortality

Since many of the babies were dead in utero at the time of admission to the hospital and since 40 of the babies weighed less than 4 pounds, the uncorrected mortality rate of 24.6 per cent is less than had been anticipated (Tables IX and X). There is little doubt, however, that even this could be reduced by more prompt recognition of the significance of the symptoms by both patient and physician.

TABLE IX. GROSS FETAL MORTALITY FROM ABRUPTIO PLACENTAE

Total No. of cases of abruptio placentae	390*	
Total No. of fetal deaths	96	
Total uncorrected fetal mortality		24.6%
Stillborn	49	
Neonatal deaths	47	
Corrected fetal mortality		14.3%

\*Includes 7 sets of twins.

†Forty of the 96 dead babies weighed less than 4 pounds.

Table X. Fetal Mortality According to Method of Delivery in Cases of Abruptio Placentae

	NO. OF CASES	NO. OF FETAL DEATHS	% FETAL DEATHS
Vaginal delivery	271	60	22.1
Cesarean section	114	36	31.6

Review of these cases of premature separation of the placenta will establish, we believe, the following principles concerning this complication:

- 1. If the case be one of mild degree, the conduct of labor should be unaltered except for the administration of oxygen and increased vigilance on the part of the obstetrician.
- 2. In the more severe instances, the best interests of both mother and baby are served by as prompt evacuation of the uterus as is compatible with safety, particularly in those cases in which there is an associated fibrinogenopenia.
- 3. Treatment for shock and replacement of blood before measures for delivery are instituted decrease the operative risk.
  - 4. Replacement of blood following delivery is essential.
  - 5. Precaution must be taken against postpartum hemorrhage.

#### Part II. Placenta Previa

During the same 14 year period there were 169 cases of placenta previa on our service in the Pennsylvania Hospital. Included are only those cases which occurred beyond the twenty-eighth week of pregnancy and in which the diagnosis was established by palpation of the placenta through the cervix, its visualization by roentgen studies, or by confirming its low attachment

at the time of cesarean section. By observance of these criteria, many instances of mild painless bleeding were eliminated from the study even though it is likely that low implantation of the placenta was present in some. It may well be that the bleeding in some of these patients was due to rupture of the marginal sinus, a diagnosis which we have not been able to make with any degree of certainty prior to delivery.

The recorded incidence of placenta previa varies with the strictness of the criteria for its diagnosis. In our material, limited to proved cases, the incidence was one in 248 deliveries (Table XI).

TABLE XI. INCIDENCE OF PLACENTA PREVIA

Total No. of deliveries	41,919	
No. of cases of placenta previa	169	
Incidence of placenta previa	1 in 248	

Low implantation without actual encroachment on the internal os was the degree most commonly encountered (Table XII). Next in order of frequency were the total and partial varieties.

TABLE XII. TYPES OF PLACENTA PREVIA

	NO.
Total	23
Partial	20
Low implantation	113
Low implantation Not stated	13

#### Management of Placenta Previa

Our choice of treatment in placenta previa is dependent upon the severity of hemorrhage, the degree of shock, the likely viability of the child, the location of the placenta, the presentation, and the amount of cervical dilatation.

In former years the diagnosis of or even a strong suspicion of placenta previa was considered an indication for immediate delivery. This attitude was attended by a high percentage of premature deliveries with an inevitably high rate of fetal mortality. Following the work of MacAfee, Herman Johnson, and the late Tiffany Williams, we adopted the so-called expectant treatment of placenta previa. Patients who present this complication prior to the thirty-eighth week of pregnancy are treated expectantly unless the bleeding is alarming in amount or duration. In most instances the first bleeding will cease spontaneously if the patient is kept in bed. Vaginal examination except by speculum is avoided prior to the thirty-eighth week because of the danger that digital dislodgment or perforation of the placenta may force the necessity of premature delivery. Because of the tendency of subsequent hemorrhages to be increasingly profuse, expectantly managed patients should remain in the hospital until delivered.

If the bleeding occurs during labor, if the placenta is marginal or lateral, and if the presentation is polar, rupture of the membranes often will allow the presenting part to make sufficient pressure on the partly separated and traumatized placenta to control the bleeding. Traction on the scalp occasionally is advisable. In such instances labor is allowed to proceed to spontaneous or low forceps delivery. If the cervix is completely dilated and if the baby is small, version and extraction on rare occasions may be the

e

y - - e

procedure of choice except in the presence of central implantation. Because of the danger that deep laceration of the cervix may extend into the placental site, manual dilatation of the cervix is strictly contraindicated.

By following these principles, we were able to deliver 51 (30.1 per cent) of our patients by the vaginal route (Table XIII).

TABLE XIII. METHODS OF DELIVERY IN PLACENTA PREVIA

	CASES	%
Vaginal delivery	51	30.1
Forceps	22	
Spontaneous	25	
Version and extraction	2	
Breech extraction	1	
Braxton Hicks version	1	
Cesarean section	118	69.9
Total No. of cases	169	100.0

In 118 (69.9 per cent) of our cases, cesarean section was performed. If the bleeding is profuse and the cervix is closed, we believe that the best interests of both mother and child are served by this procedure. Regardless of the amount of cervical dilatation, cesarean section is done in every case of central placenta previa and in most instances of malpresentation.

### Maternal Mortality

There was no deaths among the 51 patients in whom the amount of cervical dilatation and other favorable factors permitted vaginal delivery. Unfortunately, a relatively small number were found amenable to such simple management. No maternal mortality attended the 118 cesarean sections (Table XIV).

TABLE XIV. MATERNAL MORTALITY FROM PLACENTA PREVIA

Cases of placenta previa	169
Maternal deaths from placenta previa	0 (0.0%)

#### Fetal Mortality

Intrauterine asphyxia presumably was responsible for most of the fetal deaths and was, no doubt, a contributory cause in all of them (Table XV). Prematurity was the next most frequent factor as 11 of the 19 babies who died weighed less than 4 pounds.

TABLE XV. GROSS FETAL MORTALITY ACCORDING TO METHOD OF DELIVERY

	DEATHS	CASES	% MORTALITY
Vaginal delivery	8	51	15.7
Cesarean section	11	120*	9.2
Total fetal mortality	19	171	11.1
Corrected fetal mortality			4.2

\*Included 2 sets of twins.

†Eleven of 19 dead babies weighed under 4 pounds.

Our experience has resulted in adoption of the following principles in the management of placenta previa:

1. Accurate diagnosis of the cause of bleeding is desirable. A cautiously performed vaginal examination, preferably with a speculum only, may reveal that the bleeding is due to a cervical polyp, an erosion, or, rarely, a cervical carcinoma rather than to placenta previa. Examination, however, entails the danger of sudden profuse bleeding as well as the risk of infection. No patient suspected of having placenta previa should be examined until she is in an operating room which is ready for both vaginal and abdominal delivery. Rectal examination has no place in the management of this complication; it is attended by great likelihood of producing hemorrhage and gives less accurate information than one can obtain by vaginal examination.

X-ray studies by the "soft tissue" technique have been valuable in localization of the placenta. By this method the normally situated placenta is visualized in practically all cases; the low-lying placenta is hidden by the pelvic bones. Failure to find the placental shadow high in the uterus is definite evidence that the placenta is located probably, but not necessarily, in the lower uterine segment. The technique is dependable, therefore, only in ruling out, rather than positively diagnosing, placenta previa. This method of study is applicable, obviously, only in those patients in whom bleeding has subsided.

2. Treatment of shock and replacement of blood are essential before procedures for delivery are instituted.

3. Expectant management of patients with placenta previa in the hope of bringing the child to greater viability is advisable provided the patient remains in the hospital throughout the remainder of the pregnancy.

4. If the cervix is dilated and the placenta previa is only partial or marginal, rupture of the membranes often will allow the presenting part to make sufficient pressure on the placenta to stop the bleeding.

5. Because of the danger of profuse hemorrhage from the vessels of the placental site and the added risk of infection, manual dilatation of the cervix and forcible vaginal delivery have no place in the treatment of this condition.

6. The hydrostatic bag has no place in the management of placenta previa; the hazard of hemorrhage incident to its insertion and several instances of continuing, concealed intrauterine bleeding following its insertion have resulted in our giving up its use.

7. In all cases in which the cervix is not dilated, in all instances of central placenta previa regardless of the degree of cervical dilatation, and in those of malpresentation of the fetus, cesarean section is the safest and therefore the most conservative form of treatment. The fetus, as well as the mother, may lose blood through the separated and damaged placenta. Incision through the placenta may produce additional fetal hemorrhage. For these reasons classical cesarean section is preferred to the low cervical operation.

8. The use of oxytocin in dilute solution intravenously by continuous drip immediately after delivery lessens the danger of postpartum hemorrhage.

#### References

- Dieckmann, W. J.: Am. J. Obst. & Gynec. 31: 734, 1936.
   Hertig, A. T.: Clinics 4: 602, 1945. (Cited by Greenhill.)
   Weiner, A. E., Reid, D. E., and Roby, C. C.: Am. J. Obst. & Gynec. 66: 475, 1953

807 SPRUCE STREET, PHILADELPHIA, PA.

### SUPERIMPOSED TOXEMIA, ABRUPTIO PLACENTAE, HYPOFIBRINOGENEMIA, ACUTE RENAL SHUTDOWN, AND PARALYTIC ILEUS COMPLICATING A CASE OF PREPREGNANCY HYPERTENSION

JOHN F. J. CLARK, M.D., AND RIDGELY BENNETT, M.D., WASHINGTON, D. C.

(From the Department of Obstetrics and Gynecology, Howard University School of Medicine and Freedmen's Hospital)

THE responsibility in the field of obstetrics to decrease the maternal death rate and morbidity has increased with the growing population and the yearly birth rate of over 4 million. The three major causes which account for 90 per cent of all maternal deaths are hemorrhage, toxemia, and infection. Obstetricians striving to decrease the maternal mortality rate should report their experiences with problem cases. Two of the primary causes of maternal deaths, hemorrhage and toxemia, were involved in the case below.

The patient had prepregnancy hypertension that was complicated by superimposed toxemia, abruptio placentae, hypofibrinogenemia, acute renal shutdown, and paralytic ileus.

A 33-year-old para i, gravida ii, whose last normal menstrual period was Aug. 10, 1956, was hospitalized on March 10, 1957, because of albuminuria, elevated blood pressure, and marked weight gain. Prior to hospitalization, the patient had been placed on reserpine and a salt-free diet, later on reserpine-hydralazine hydrochloride.

TABLE I. THE PRENATAL COURSE

	11/12/56	12/11/56	1/11/57	2/11/57	2/22/57	3/8/57
Blood pressure Weight Albumin	143/80 153 Negative	130/70 158 Negative	140/100 164 Negative	160/100 178 Negative	170/100 175 Negative	180/100 187

The blood pressure had been elevated during the last trimester of her first pregnancy in 1948.

Physical examination on admission showed a blood pressure of 180/110, slight exophthalmos, a transverse lie of the fetus, and fetal parts easily palpable. The fetus was the size of a 31 weeks' gestation, and the fetal heart tones were 144. There was 3 plus pitting edema of the extremities and 2 plus albuminuria. The impression was that she had prepregnancy hypertension with superimposed toxemia.

The patient was placed on a hypertensive salt-free diet, diuretics, hypotensive drugs, and pentobarbital sodium. On March 11, 1957, the blood pressure was 182/120, albuminuria 4 plus. There was facial and finger edema, edema of the anterior abdominal wall, and 3 to 4 plus pitting pretibial edema. On March 12 the blood pressure was 182/120, edema of the

extremities was 2 plus, the eyegrounds showed vasconstriction, and urinalysis showed 3 plus albuminuria. On March 13, the patient's blood pressure was 220/138. She began to experience vaginal bleeding and complained of blurred vision. Urinalysis showed 4 plus albuminuria.

The membranes were ruptured in an attempt to initiate labor. The impression at this time was that there was a mild premature separation of the placenta. Six hours later the patient was bleeding moderately and having uterine contractions. The cervix was dilated 4 cm., the clotting time was normal, and bilateral papilledema was noted. The bleeding began to increase and a low segment cesarean section was performed. At operation several myomas and a Couvelaire uterus were found. The peritoneal cavity contained approximately 300 c.c. of serosanguineous fluid. A 3 pound, 4 ounce stillborn female infant and a placenta which had completely separated were delivered.

The repeated clotting time determination immediately after operation was normal. The clot when incubated at 37° C. fragmented in 30 minutes. Soon after arrival on the ward the patient's blood pressure and pulse were unobtainable, oozing from the abdominal incision was noted, and the wound dressing was half soaked with blood. She developed hypofibrinogenemia and was treated with prednisone, antihemophilic plasma, firinogen, blood, and fresh plasma.

On the first, second, and third postoperative days the total urinary output was 80, 65, and 35 c.c., respectively. The nonprotein nitrogen rose to 170 mg. per cent and creatinine to 16.8 mg. per cent. Lower nephron nephrosis developed and was treated with closely supervised fluids and electrolytes. A cecostomy was performed on the ninth postoperative day for adynamic ileus because volvulus of the sigmoid could not be ruled out. The liver was very slow in recuperating to form fibrinogen because at this time she bled profusely from the skin incision. The hemoglobin rose from a low of 5.1 Gm. to 10.4 Gm. and the hematocrit rose from a low of 14 to 34. Urinary output and blood chemistry values returned to normal. Funduscopic examination revealed a well-formed disc with arteriosclerotic changes. She was hospitalized a total of 30 days.

The patient was followed closely by an internist after discharge from the hospital. She had disturbances of equilibrium which in 6 months had completely disappeared. The blood pressure had returned to 140/90, but she constantly had albuminuria. Intravenous pyelography showed bilateral polycystic kidneys.

#### Comment

Prepregnancy hypertension difinitely is a predisposing factor to toxemia of pregnancy, and with superimposed toxemia the incidence of abruptio placentae increases. This patient developed superimposed toxemia which did not respond to conservative measures, and she progressed to severe abruptio placentae.

In the past two decades, maternal mortality has been reduced remarkably but deaths from obstetrical hemorrhage have not decreased proportionately. With severe abruptio placentae, when the clotting mechanism has been altered, the patient's condition cannot be stabilized with blood transfusions alone. Fibrinogen must be administered.

The theories of the disturbance in the clotting mechanism are: (1) A thromboplastin-like substance arising from the uterus produces intravascular clotting with consumption of fibrinogen.<sup>1</sup> (2) A fibrinolysin is increased which is active against fibrinogen and fibrin.<sup>2</sup> DeLee,<sup>3</sup> in 1901, first called our attention to uncontrollable hemorrhage associated with abruptio placentae. Dieckmann,<sup>4</sup> in 1936, noted that there was a reduced level of fibrinogen in patients who bled profusely with severe abruptio placentae. Hypofibrinogenemia has been detected in one-third to one-half of the patients with severe forms of abruptio placentae.<sup>5</sup>

The clot observation test has proved to be a rapid and practical aid. Normally a clot forms in 8 to 12 minutes and remains clotted for 24 hours. In

hypofibrinogenemia no clots form or there is complete dissolution of the clot in 30 to 60 minutes.5 An unstable clot may form when the fibrinogen levels are in the range of minimal values, in the presence of fibrinolysin or as a result of both of these factors.<sup>5</sup> The most practical test, which was applied initially in this case, is the clotting time. If a clot forms, normally it is allowed to remain in the tube at 37° C. for an hour with frequent observations for evidence of lysis which is manifested by dissolution of the formed clot.

#### Summary

This case exemplifies the numerous problems that can occur in a pregnant woman with prepregnancy hypertension on which is suddenly superimposed toxemia of pregnancy. An alteration in the clotting mechanism was constantly watched for. Acute renal shutdown was one of the complications we were concerned with after the episode of bleeding and the period of shock which might cause damage to the pituitary, brain, and kidney. Paralytic ileus that developed after the anuria possibly could be explained by bleeding into the peritoneal cavity. It is not an uncommon factor. Ruling out whether or not the patient had a volvulus of the sigmoid was another problem.

#### References

- 1. Schneider, C. L.: Surg. Gynec. & Obst. 92: 27, 1951.

- Reid, D. E., Roby, C. C., and Weiner, A. E.: J. A. M. A. 161: 1244, 1956.
   DeLee, J. B.: Am. J. Obst. 44: 785, 1901.
   Dieckmann, W. J.: Am. J. Obst. & Gynec. 31: 734, 1936.
   Weiner, A. E., Reid, D. E., and Roby, C. C.: Am. J. Obst. & Gynec. 66: 475, 1953.

# DEATHS FROM ASIAN INFLUENZA ASSOCIATED WITH PREGNANCY

D. W. Freeman, M.D., and A. Barno, M.D., MINNEAPOLIS, MINN.

(From the Minnesota Maternal Mortality Committee)

ELEVEN deaths from Asian influenza associated with pregnancy occurred in the recent epidemic in Minnesota. Eight deaths occurred in a 10 day period in late October and early November, 1957, and one each in December, 1957, January, 1958, and March, 1958. In the eighth year of the present study of maternal deaths in Minnesota extending from April 1, 1957, through March 31, 1958, there were a total of 57 deaths from all causes associated with pregnancy. Influenza accounted for more deaths than any other cause and for 19.2 per cent of the total.

Each of the 11 deaths was studied in detail by an investigator for the Maternal Mortality Committee and the data relating to each were critically evaluated by the committee. Details pertaining to the operation of the Maternal Mortality Study in Minnesota have been previously described.<sup>1</sup>

#### Clinical Course and Findings

The age range of the patients was from 19 to 35. Three were primigravidas and 8 multiparas. Three of the deaths occurred in the second trimester of

pregnancy, 7 in the third, and one 5 weeks post partum.

All of the patients died of respiratory insufficiency associated with an overwhelming pulmonary edema and pneumonia. This was demonstrated by clinical and autopsy findings in 9 cases and by clinical evidence in the other 2, including a chest x-ray examination in one. In 8 cases the patients experienced typical "flulike" symptoms for from one to 10 days before the onset of severe respiratory difficulty. Six of these had such symptoms for 4 days or less, one for one week, and one for 10 days. Following the onset of pulmonary symptoms the course was a very fulminant one characterized by fever, marked respiratory difficulty, cough productive of large volumes of bloody sputum, prostration, and often cyanosis and shock. After the onset of these symptoms 6 patients died in 24 hours or less and 2 in 30 hours. Three survived 3 days each; two of these appeared to be improving on antibiotic therapy but each then developed signs of pulmonary edema and died less than 12 hours later.

There was no evidence that any treatment which was given significantly affected the clinical course. In 10 cases antibiotics were administered. Three patients were given them for less than 24 hours before death, but 7 received adequate doses of tetracycline for from 30 hours to 5 days. Three of these were also given penicillin and one, streptomycin. Three patients were given digitalis and two were given diuretics. Oxygen was administered in 8 cases.

d

y

nt

h

d

se

le

y

1-

as

f

n

y

er

X-

et

rs

1-

y

of

et ee

ic ss

ly ee

d

se

en es. It is interesting to note that no influenza vaccine had been given to 10 of these patients. Information regarding this point was not available in the other case.

Pulmonary edema and pneumonia were found in all 9 patients who were autopsied and gross pulmonary hemorrhage was evident in 7. In 3, hyaline membrane formation was described, and one showed abscess formation. Other autopsy findings included the presence of pleural fluid in 8 patients. This was described as minimal in one, 200 to 500 c.c. on each side in 5, and from 1,000 to 1,500 c.c. in 2. Mitral stenosis was demonstrated in one case.

Isolation of the Asian strain type A influenza virus from the lung was successful in 3 of the 4 patients in whom it was attempted. Coagulase-positive staphylococci were cultured from the lungs in 2. Nonpathogenic bacteria were isolated from pulmonary secretions in 2, and a blood culture in another was sterile. No cultures were taken in the remaining 3.

#### Frequency of Influenza Deaths in Pregnancy

The reporting of cases of influenza is known to be poor and no data pertaining to the incidence of influenza in pregnancy have been collected in Minnesota. However, the total number of deaths from influenza as reported by the section of Acute Communicable Diseases of the Minnesota Department of Health indicates that there were 246 deaths in the state attributed to or associated with influenza in the period August through December, 1957.2 This total was arrived at by including (1) all deaths reported with influenza as cause of death, 165 deaths; (2) deaths attributed to other causes but mentioning influenza on the death certificate, 59 deaths; (3) histories received in the Division of Disease Prevention and Control indicating that influenza was the cause of death, 22 deaths. Of these 246 deaths, 16 occurred among women in the age group 15 to 45. Two deaths in the Maternal Mortality group being reported occurred after December, 1957, and one 5 weeks post partum. Thus, there were 8 pregnant women who died in the August-December time period, which means that 50 per cent of the women in the childbearing age who died of influenza in Minnesota were pregnant.

There are only occasional other reports in the literature which indicate that the mortality rate from influenza is higher among pregnant women than among other individuals. Greenberg and associates<sup>3</sup> found that 10 per cent of 216 deaths from Asian influenza in New York City occurred in pregnant women and that nearly one-half of all women in the childbearing age who died were pregnant. A report by the Public Health Laboratory Service in England noted that 12 of 103 deaths in women, ages 15 through 44, occurred in pregnant women. This was considered about double the expected number.<sup>4</sup> A highly significant increase in the fatality rate from influenza in pregnant women as compared with nonpregnant women in the same age group would appear to be demonstrated by these reports.

#### Mechanism of Death

Reports on the pandemic of Asian strain influenza indicate that deaths occurred either following a secondary bacterial infection or as a result of a fulminating edematous pneumonia. The greater number occurred in patients whose course was complicated by bacterial infections, usually a pneumonia but occasionally a severe membranous tracheobronchitis. Deaths occurred in this group in patients with chronic debilitating disease, other poorrisk groups, following infection with antibiotic-resistant organisms which were usually staphylococci, and in inadequately treated patients. A second

and substantially smaller group of deaths resulted from an overwhelming wet pneumonia, usually hemorrhagic and very fulminating in its development and course. At autopsy, no significant bacteria were isolated and the deaths were usually attributed to virus pneumonia. The actual mechanism of death in this group was respiratory insufficiency resulting from the pulmonary edema.

All 11 cases in this series fell into the second group. Significant bacteria were isolated from the lung at autopsy in 2 cases, but these patients also demonstrated an overwhelming pulmonary edema. Pregnant women are known to be susceptible to the development of pulmonary edema under other circumstances.<sup>7</sup> The tendency demonstrated here of pregnant patients to develop pulmonary edema in association with influenza much more frequently than nonpregnant individuals would appear to be another manifestation of this susceptibility. In this connection it is of interest to note that an unusually high occurrence of rheumatic heart disease, especially mitral stenosis, has been found in association with this type of influenza death.<sup>3, 4, 8</sup> Peripheral vasoconstriction has been demonstrated in patients suffering from influenza and it has been suggested that such vasoconstriction may displace excess quantities of blood into the pulmonary vascular bed.<sup>9</sup> In patients subject to pulmonary congestion such displacement may be sufficient to precipitate acute pulmonary edema.

#### Prophylaxis

Partial protection against influenza is afforded by presently available vaccines and there is reason to hope for the development of more completely effective preparations in the future. Routine administration of such vaccine to pregnant patients may well be indicated in view of the apparent increased susceptibility of such patients to severe pulmonary complications. This would appear to be most clearly indicated during influenza epidemics but it should not be forgotten that the problem of influenza is a perennial one. Influenza appears sporadically as well as in pandemics and local epidemics. The disease has had an impact on mortality figures in Minnesota on 11 occasions since 1919. The most recent epidemic (Asian variety) was better advertised, but according to Langmuir, as measured by excess influenza pneumonia mortality, it was only slightly more severe than the influenza A' epidemic of 1953 and considerably less severe than the influenza A epidemic of 1943.

Prophylactic measures directed at attempting to prevent the development of pulmonary edema would appear to be indicated in pregnant women suffering from influenza. Should signs of pulmonary edema develop, prompt and vigorous treatment is indicated.

#### Summary

- 1. Clinical and autopsy findings in 11 deaths from Asian influenza associated with pregnancy are described. These deaths were all evaluated by the Minnesota Maternal Mortality Study Committee.
- 2. Asian influenza was the leading cause of maternal mortality in Minnesota in 1957.
- 3. Fifty per cent of deaths from Asian influenza in Minnesota among women of childbearing age occurred in pregnant women.
- 4. The deaths associated with pregnancy were all characterized by fulminating and overwhelming edematous pneumonia with respiratory insufficiency

it 18

h

ia

0

e. J.

0

y f 1-

0-

m 98

ts

0

le y en-S. CS al in tata ie

pen pt

·j-1e

e-

ıg

11cy

as the immediate cause of death. This is in contrast with deaths due to influenza reported in nonpregnant individuals where secondary bacterial infections account for a large proportion.

5. The value of routine vaccination of pregnant women with suitable influenza vaccine has been discussed.

#### References

- 1. McKelvey, J. L., and Freeman, D. W.: Am. J. Obst. & Gynec. 68: 29, 1954. 2. Nelson, C. B.: Personal communication.
- Greenberg, M., Jacobziner, H., Pakter, J., and Weisel, B. A. G.: Am. J. Obst. & Gynec. 76: 897, 1958.
- Public Health Laboratory Service: Brit. M. J. 2: 915, 1958.
   Influenza Study Group, Armed Forces Epidemiological Board and Committee on Influenza, National Health Services, Santiago, Chile: J. A. M. A. 167: 290, 1958.
   Editorial: Brit. M. J. 2: 434, 1958.

- 7. Goldmann, M. A., and Primiano, N. P.: Am. J. Obst. & Gynec. 65: 314, 1953.

  8. Hers, J. F., Goslings, W. R. O., Masurel, N., and Mulder, J.: Lancet 2: 1164, 1957.

  9. Walsh, J., Burch, G. E., White, A., Mogabgab, W., and Dietlein, L.: Ann. Int. Med. 49: 502, 1958.
- 10. Meiklejohn, G., and Morris, A. J.: Ann. Innt. Med. 49: 529, 1958.
- 11. Langmuir, A. D.: Ann. Int. Med. 49: 483, 1958.

4959 EXCELSION BLVD.

MINNEAPOLIS, MINN.

# PREGNANCY COMPLICATED BY PREVIOUS BILATERAL TOTAL ADRENALECTOMY

WILLIAM J. ESTRADA, M.D., R. Z. HUNDLEY, M.D., J. E. NORRIS, M.D., AND T. G. GREADY, M.D., HOUSTON, TEXAS

(From the Departments of Obstetrics and Medicine, Hermann Hospital)

SEVERAL articles have appeared in the past few years concerning the relationship of the adrenal glands and pregnancy. Most of these have dealt with Addison's disease or hypofunction of the adrenal gland in association with pregnancy. Reports concerning patients with previous total bilateral adrenalectomy are extremely rare; only 4 are known to us. Schneider, Weed, and Bowers<sup>12</sup> reported 2 cases; one case was reported by Worner and Mathew<sup>14</sup>; and one was reported by Hunt and McConahey.<sup>6</sup>

With improved diagnostic procedures and surgical techniques these cases will gradually become more common. Since the advent of cortisone and modern substitutional therapy for adrenal hypofunction (adrenalectomy), these patients may be expected to live longer and enjoy greater fertility.

The history and management of this case and the laboratory findings are presented in detail because of the rarity of these associated conditions, and also to show the relative ease with which such patients can be carried through pregnancy.

#### Case Report

Mrs. J. T. (No. H. H. 56-16559), a 21-year-old white married woman, para 1-0-0-1, was referred to Hermann Hospital in June, 1956, with nausea and vomiting of pregnancy and a history of previous bilateral total adrenalectomy.

On admission, she did not appear to be in acute distress. Her blood pressure was 90/60, pulse 88 per minute, and respirations 20 per minute. She had a full face, increased facial and body hair, and weighed 155 pounds. Examination showed the head and neck to be normal. The heart and lungs were normal. A slight buffalo hump was present. Abdominal examination revealed scars in both flanks and the lower mid-abdomen. Pelvic examination revealed enlargement of the uterus compatible with a gestation of about 6 weeks, and otherwise normal findings. The Rh was positive, the serologic test for syphilis was positive (*Treponema pallidum* immobilization test negative), the chest x-ray was normal, and the pelvis was clinically contracted.

Past History.—On Jan. 19, 1956, the patient was admitted to another Houston hospital with a history of increased hair growth over the face, arms, abdomen, back, breasts, and thighs since the age of 17 years. She had always been overweight and during the last 2 months of 1955 had gained 20 pounds. Her blood pressure had shown gradual elevation until it reached 170/100 during January, 1956. The glucose tolerance curve was normal. Earlier in the disease the 24 hour urinary 17-ketosteroid levels were reported as 11.9 and 13.9 mg. Her menstrual history had not changed, remaining a 28 to 29 day cycle with a 4 day average flow.

Examination in January, 1956, revealed an obese white woman with a full face, increased hair growth over the body, a moderate buffalo hump, mild acne, and well-developed breasts with little glandular tissue. No plethora was noted. The blood pressure was recorded as 170/100. Significant laboratory results on this admission were reported as follows: serum potassium 6.4 mEq. per liter, serum sodium 146 mEq. per liter, urinary 17-ketosteroids 24 mg. per 24 hour urine specimen (normal 7-12), urinary 17-hydroxycorticosteroids 22 mg, per 24 hour urine specimen (normal 5). ACTH test revealed control plasma of 17-hydroxycorticosteroids at 10 mg. per cent (normal 13), and after the administration of 25 mg. ACTH intravenously over a 4 hour period this rose to 119 mg. per cent (normal 25 to 30). Chest and skull x-rays were normal.

On Jan. 31, 1956, a bilateral total adrenalectomy was performed and both adrenal glands were noted to be greatly enlarged. The histopathologic examination was reported to show "adrenal hyperplasia." At the time of operation both tubes and ovaries were noted to be grossly normal. The postoperative course was uneventful and the patient was discharged on the tenth postoperative day on 12.5 mg. cortisone per os, 3 times daily. She again was admitted to the same hospital on March 6, 1956, because of a urinary tract infection, and responded well to therapy. Following operation, the patient lost weight, her hair decreased in amount, the menses remained normal, the blood pressure dropped to normotensive levels, and in general she felt much better.

Present Illness.—The patient developed severe nausea and vomiting in June, 1956, and was treated by her physician in his office with intravenous fluids and intramuscular cortisone. Her last menstrual period was May 6, 1956, and in June a pregnancy test was reported as positive. Because of her financial status, she was referred to the Hermann Hospital Clinic Service on June 29, 1956. Just prior to her referral, she had been placed on intramuscular cortisone, 100 mg. daily, and on fluorohydrocortisone, 0.2 mg. daily. She had received DOCA (desoxycorticosterone acetate), but for an unknown period of time.

There had been treatment on 3 occasions for a positive serologic test for syphilis: this apparently was a "false positive" reaction since the TPIT was negative. She had a normal pregnancy in 1952 which terminated in cesarean section because of cephalopelvic disproportion. There was also a history of an appendectomy in 1954, and excision of a pilonidal sinus in October, 1955.

The family history was essentially noncontributory and a review of systems revealed only myopia and chronic constipation.

The immediate problem on admission was the maintenance of a normal electrolyte and fluid balance in the presence of persistent nausea and vomiting. Laboratory tests on admission revealed: hemoglobin, 12.4 Gm., hematocrit 37 per cent, white blood count, 7,450, and a normal differential count. Urinalysis was within normal limits. Electrolyte studies on admission and follow-up and other tests are included in Table I.

TABLE I. BLOOD CHEMISTRY DETERMINATIONS AND OTHER TESTS

				DATE			
	6/29/56	6/30/56	7/2/56	7/6/56	7/10/56	7/11/56	7/13/56
Serum:							
Chlorides (mEq./L.)	97.2	104.0	95.2	96.2	86.3	106.5	103.5
Carbon dioxide (vol. %)	40.0	43.8	47.5	40.0		42.8	44.7
Potassium (mEq./L.)	3.7	3.8	4.5	4.4	4.6	3.6	3.8
Sodium (mEq./L.)	139	143		132	118	122	135
Blood urea nitrogen							
(mg. %)				10	48.5	14	11
Sugar			86	80			
Fantis test (urine)							
(mEq./L.)						30	43
Circulating eosinophils						00	40
(C.mm.)				67			

Treatment.—On admission, 1,000 c.c. of 5 per cent glucose in normal saline was given intravenously, with 50 mg. hydrocortisone hemisuccinate added. This was supplemented with cortisone 50 mg. intramuscularly every 8 hours. Desoxycorticosterone acetate (DOCA), 5 mg., was given daily, and Potassium Triplex, 1 dram 3 times daily. On the third hospital day, DOCA was decreased to 5 mg. every other day and cortisone to 50 mg. twice daily. On the fifth hospital day, DOCA and cortisone were discontinued when it was decided that maintenance with Meticorten would be attempted in order to evaluate this drug. Accordingly, Meticorten, 5 mg. 4 times daily, was started. Seven days later (twelfth hospital day), the patient began vomiting, had a chill, and "felt fainty." She was immediately given 1,000 c.c. of normal saline and DOCA, 5 mg. intramuscularly, with 1 Gm. sodium chloride orally. In addition, 100 mg. hydrocortisone hemisuccinate in 1,000 c.c. of 5 per cent glucose in normal saline was given. The Meticorten was discontinued. (The chlorides and sodium serum levels were noted to be low.) On the following day (thirteenth day), cortisone therapy, 20 mg. every 6 hours, was reinstituted with sodium chloride, 2 Gm. 3 times daily. Fluorohydrocortisone, 0.1 mg. daily, was started on the fourteenth day, and salt decreased to 1 Gm. 3 times daily. She was discharged on the sixteenth day on hydrocortisone, 20 mg. every 8 hours, fluorohydrocortisone, 0.1 mg. daily, and sodium chloride.

On July 26, 1956, the patient was seen in the outpatient clinic complaining of swelling of the ankles. The supplementary salt was stopped and the hydrocortisone was decreased to 20 mg. twice daily. Throughout the remainder of her pregnancy she was continued on these same medications. Twice, she developed a cold with some purulent sputum and was treated with oxytetracycline. The electrolytes on Oct. 31, 1956, were as follows: chlorides 101.2, sodium 144, and potassium 4.9 mEq. per liter. The patient did very well following her initial hospital admission, and gained only 12 pounds during pregnancy. She was followed weekly in both the obstetrical and endocrine clinics. The urine remained free of albumin, the blood pressure was stable, and the hemoglobin remained between 12 and 13 Gm.

The expected date of confinement was Feb. 10, 1957, and she was admitted to the hospital on January 22 for study and preparation for therapy in regard to proposed delivery by repeat cesarean section. Blood studies showed: sugar 81 mg. per cent chlorides 95 mEq., sodium 138 mEq. potassium 3.4 mEq. per liter, and carbon dioxide combining power 42.8 vol. per cent. It was felt that the fetus was small so operation was postponed and the patient was readmitted on Feb. 4, 1957. A low transverse cesarean section was performed under spinal anesthesia on February 7, with delivery of a male infant in good condition, weighing 7 pounds, 11 ounces. A Pomeroy type tubal sterilization was performed.

TABLE II. LABORATORY STUDIES FOLLOWING CESAREAN SECTION

		DA	TE	
	2/8/57	2/9/57	2/10/57	2/11/57
Blood.—				
Serum chlorides (mEq./L.)	110	105		
Potassium (mEq./L.)	4.5			
Sodium (mEq./L.)	136			
Carbon dioxide combining power				
(vol. %)	37.2	42.8		
Hemoglobin was 12.6 Gm. and hema- tocrit 38 per cent				
24 Hour Urine.—				
Volume (c.c.)	1700	1390	1110	2660
Chlorides (mEq./L.)	5430	2223	1026	684
Potassium (mEq./L.)	24	65	53	33
Sodium (mEq./L.)	48	118	56	46
Urinalysis was within normal limits				

The baby was followed closely and had no complications.

The patient was given the usual preoperative medications and 30 minutes before operation 1,000 c.c. of 5 per cent glucose in distilled water was started with 100 mg. of hydrocortisone hemisuccinate added. During the procedure, she was also given 500 c.c. whole blood. Postoperatively, cortisone acetate, 25 mg. intramuscularly every 8 hours, and

1179

1,000 c.c. of 5 per cent glucose in normal saline with 40 mEq. of potassium chloride were given. On the first postoperative day intramuscular cortisone acetate was decreased to 12.5 mg. every 8 hours, and oral medication was begun. This consisted of hydrocortisone 20 mg. twice daily, and fluorophydrocortisone 0.1 mg. daily. Intramuscular cortisone was discontinued on the third postoperative day and she was discharged on the eighth postoperative day.

The patient returned for a checkup 6 weeks later and was doing well. She was continued on the same medications.

TABLE III. HORMONE ASSAYS

	DATE						
	8/18/56	11/6/56	12/6/56	1/29/57	POST PARTUM		
					2/19/57	3/23/57	
Week of gestation	15	26	30.5	38	1.5	6	
17-ketosteroid level (N 5-15) mg./24 hour urine	9.0	21.4	17.0	8.0	11.2	6.7	
17-ketogenic (N 4-12) mg./24 hour urine	12.7	19.0	6,5	21.0	10.0	8.7	
Pregnanediol (N non-preg. 0.5) (N preg. 14-16) mg./24 hour							
urine	16.0	_	2.4	0	-	5.1	
11-oxycorticosteroids (N 0.1-0.5) mg./24 hour urine	_	0.39	0.84	0.84	0.4	0.7	

#### Comment

The relative ease with which this patient was managed demonstrates that our apprehension at the onset was unwarranted. DOCA was discontinued early because it is an antidiuretic substance and produces a decrease in filtration rate at the glomerulus, an increase in sodium reabsorption, and a subsequent decrease in urinary output.<sup>2</sup> Fluorohydrocortisone, by virtue of its salt-retaining properties, was used to avoid unnecessary additional dietary salt. Meticorten was discontinued early since the patient's condition deteriorated on this medication. Meticorten is not a physiological adrenal steroid and has certain actions different from those of cortisone or hydrocortisone, which are naturally secreted adrenal glucocorticoids.

As demonstrated, the patient did quite well on hydrocortisone and fluorohydrocortisone, via the oral route, without parenteral medication. During stress, 13 such as surgery and labor, 4 the rate of production of adrenal hormones is increased and is usually reflected by a rise in plasma levels. Therefore, supportive therapy was included during operation and the immediate postoperative period in the form of intravenous and intramuscular adrenocorticosteroids.

An increased activity of the adrenal cortex is seen in the normal pregnant woman, which is shown by increased urinary steroids. In the woman with adrenal deficiency (Addisonian), increased urinary steroids are also found. 5, 11

The question arises as to the origin of the increased urinary steroids. Some investigators feel that the placenta may be the site of origin,<sup>6, 7, 8, 10</sup> and with this, Jailer<sup>7</sup> mentioned that in pregnant patients with adrenal hypofunction the placenta can partially substitute for the adrenal gland, particularly in the third trimester. Recently, however, Hills and co-workers,<sup>5</sup> Kaiser,<sup>11</sup> and Baulieu and associates<sup>3</sup> have shown that there is no significant fetal or placental steroid support during pregnancy, i.e., no production of cortisone or hydrocortisone.

Hills and associates<sup>5</sup> feel that the increased urinary elimination of neutral reducing lipids, 17-ketosteroids, pregnanediol, and particularly the glycogenic corticoids seen in adrenal-deficient pregnant women, suggests an enhanced

endogenous supply of adrenal-like alphaketolic steroids. Assali and Hamermesz<sup>1</sup> feel that an adrenotrophic substance, chorionic ACTH, is elaborated by the placenta and accounts for the rise in urinary steroids by increasing the activity of the adrenal cortex. This increase of steroid production in the woman with adrenal deficiency is not felt by Kaiser and Hills to be adequate replacement therapy.

Kaiser and Baulieu and co-workers have postulated that the placenta does produce progesterone, but after the twenty-fourth week Kaiser found no further increase.

In our patient, there was no adrenal gland present for stimulation and therefore we would not expect any rise in cortisone or hydrocortisone excretion. Unfortunately the hormone levels on this patient were not complete and appear to be unsatisfactory with unexplained fluctuations of the urinary hormone levels, despite maintenance on essentially the same medications throughout pregnancy. Because of this discrepancy, we are unable to make any definite conclusions as to the placenta's producing cortisone or hydrocortisone. III shows the hormone levels at different periods throughout pregnancy and the early postpartal state.\* Rechecks with the laboratory revealed no discrepancy of hormone levels in other patients on similar days. We can definitely conclude that these patients can be carried with relative ease through a pregnancy if they receive adequate replacement therapy.

This patient had Cushing's syndrome due to adrenal hyperplasia and was of Cushing's syndrome that had been treated by subtotal adrenalectomy, with treated by total adrenalectomy. Schneider and associates12 reported a case they believed, was because the adrenal gland is sensitive to stimulation during pregnancy and hence the activity increased, resulting in recurrence of the syndrome. They felt that because of this factor, in a patient with Cushing's syndrome due to adrenal hyperplasia, who might become pregnant, a total adrenalectomy was preferred over a subtotal adrenalectomy.

Although most patients with Cushing's syndrome have amenorrhea, this patient continued to have normal menses; she did not become pregnant, however, until bilateral total adrenalectomy had been performed and substitutional therapy instituted.

Because of the rarity of this condition, we were unable to anticipate the exact course of management of this patient. We hope that others may profit by this report.

#### Summary

A case of pregnancy in a patient with a previous bilateral total adrenalectomy is presented. Management by oral substitution therapy was successfully carried out, and dosages are listed. Laboratory findings and the treatment of stress complications are included. Delivery was by repeat cesarean section.

#### References

- 1. Assali, N. S., and Hamermesz, J.: Endocrinology 55: 561, 1954.
- de Alvarez, R. R.: Discussion of Hunt and McConahey.<sup>6</sup>
   Baulieu, E. E., Bricaire, H., and Jayle, M. F.: J. Clin. Endocrinol. 16: 690, 1956.
- 4. Gemzell, C. A., Ordis Robbe, H. J., and Strom, G.: Acta endocrinol. 23: 158, 1956.
- Hills, A. G., Venning, E. H., Dohan, F. C., Webster, G. D., Jr., and Richardson, E. M.:
   J. Clin. Invest. 33: 1466, 1954.
   Hunt, A. B., and McConahey, W. M.: Am. J. Obst. & Gynec. 66: 970, 1953.
   Jailer, J. W.: Bull. Sloane Hospital for Women 2: 82, 1956.

<sup>\*</sup>The studies were done by the Hycel Laboratory, Houston, Texas.

- S. Jailer, J. W., and Knowlton, A. I.: J. Clin. Invest. 29: 1430, 1950.
   Jailer, J. W., and Longson, D.: S. Clin. North America 37: 341, 1957.
   Johnson, R. H., and Haines, W. J.: Science 116: 456, 1952.
   Kaiser, I. H.: J. Clin. Endocrinol. 16: 1251, 1956.
   Schneider, G. T., Weed, J. C., and Gowers, C. Y.: Obst. & Gynec. 10: 437, 1957.
   Selye, H.: The Physiology and Pathology of Exposure to Stress: A Treatise Based on the Concepts of the General-Adaptation Syndrome and the Diseases of Adaptation, Montreal, 1950, Acta, Inc.
   Worner, K. G., and Mathew, A. G.: J. Obst. & Gynaec. Brit. Emp. 63: 248, 1956.

# THE EFFECT OF PREGNANCY ON HEPATOLENTICULAR DEGENERATION (WILSON'S DISEASE)

Report of a Case

JOHN H. BIHL, M.D., NORTHVILLE, MICH.

(From the Northville State Hospital)

CASES of hepatolenticular degeneration have attracted considerable attention during recent years, and much more has been learned about this rare disease. Some understanding of its biochemical abnormalities, clinical manifestations, and evident hereditary character now permits its interpretation as an inborn error of the metabolism. The nature of the error still remains obscure. Two different concepts of the pathogenesis of the disease have been under discussion. Uzman and co-workers<sup>12</sup> assume an unusual affinity of certain tissue proteins to copper. The primary metabolic defect consists in the formation of proteins with high copper affinity and their incomplete tissue metabolism. More favored, currently, and supported by Glazebrook,<sup>5</sup> Bearn,<sup>1</sup> Cartwright and co-workers,<sup>2, 3</sup> and Scheinberg and Gitlin<sup>8</sup> is the attempt to relate the disease to a deficiency of ceruloplasmin, a serum globulin within the alphatwo globulin fraction. Ceruloplasmin binds tightly about 95 per cent of the serum copper. It is thought that the metabolic abnormality constitutes a diminution and disturbance of the ceruloplasmin and synthesis.

The clinical picture of Wilson's disease is the result of extensive damage in tissues, especially in brain and liver. In order to establish the diagnosis, one must provide evidence of the triad of the syndrome of extrapyramidal disease (motor incoordination, rigidity, sudorrhea), cirrhosis of the liver, and the "Kayser-Fleischer ring." Invariably, it is accompanied by renal abnormalities resembling the Fanconi syndrome (amino-aciduria, negative phosphate balance, and bone disease). The psychiatric abnormality of Wilson's disease is described by Sullivan and co-workers<sup>11</sup> as being a characteristic affective disorder. It reproduces in many respects symptoms of a toxic state, however, and occasionally it seems to be transient in character. Memory and orientation appear to remain intact. The disease is hereditary in an autosomal recessive manner. The neurological syndrome or the liver trouble may prevail. The severity and prognosis depend on the latter. It is a disease of adolescence, in most cases leading to death in the third decade of life or earlier.

Thus, in theory, Wilson's disease is opposed to pregnancy in many ways. Because of the liver disease there is sexual underfunction with amenorrhea and poor chances for conception. Furthermore, the neurological symptoms constitute a serious embarrassment for marriage. Not all female patients with

Wilson's disease will reach the reproductive age, and, last but not least, the disease is less common in females than in males. In fact, described pregnancies in persons afflicted with Wilson's disease occurred either before cirrhosis of the liver became clinically overt, or terminated in early abortion. It is currently believed that female patients with a significant degree of liver impairment cannot carry a pregnancy beyond the first trimester. The present report deals with observations of a case of advanced Wilson's disease in which pregnancy was successfully carried out and terminated with the delivery of a living, normally developed, healthy full-term baby boy.

The patient, a white woman, was born in 1933. Both her parents are of Scotch extraction. The family history has been traced back several generations with the result that further hereditary evidence of Wilson's disease was found. Her parents were consanguineous, the great-grandmothers having been related. The patient's pedigree shows her to be the fourth child within a sibship of eight. An older sister died at the age of 2 from an unknown cause. Another sister died at the age of 26, and one of her brothers at the age of 19 from Wilson's disease.

At the age of 9 and again at 15, the patient was jaundiced. In 1950, at the age of 17, she first noted a tremor of the right hand and speech difficulties. Since then this has frequently recurred in an exacerbated form. In the spring of 1953 she was hospitalized because of abdominal discomfort and more dysarthria. At that time the diagnosis of Wilson's disease was established. The patient's pneumograms showed a moderate degree of dilatation of the left lateral ventricle of the brain. The protein content of the spinal fluid was increased and the gold curve was 12221000. The serum copper was normal and the daily urine copper excretion varied between 1.2 and 3.8 mg. The results of liver function studies indicated an early stage of cirrhosis. She improved after treatment with a chelating agent, dimercaprol.\* Late in 1954 the patient gained excessive weight, complained of abdominal fullness, constipation, and bleeding from hemorrhoids. The tremor and speech disorder rapidly became worse. She neglected her housework, had suicidal intentions, and apparently was bedridden for a time.

In the spring of 1955, at the age of 22, she was first seen at The Grace Hospital Outpatient Department. Physical examination at that time showed her to be fairly nourished and careless in appearance. She had a vacuous look, an open, edentulous mouth with slight drooling. There were a few follicular petechiae on the lower legs. The eyes showed a Kayser-Fleischer ring and subicteric scleras. There were wasting of the hand muscles and definite palmar erythema. The venous pattern on the abdominal wall was visible. The abdomen was protuberant and distended. The liver was down about 6 cm. below the costovertebral margin and rather firm. The spleen was not palpable and there was no physical evidence of ascites. On rectal examination bleeding hemorrhoids were found. The patient showed a marked dysarthria of scanning speech type. There was a coarse tremor of the upper extremities with an intention ataxia and "wing-beating" athetoid motions. The gait was staggering and the Romberg sign was strongly positive. There were hyperactive deep reflexes, but no pyramidal signs. Her behavior was markedly inappropriate. The remainder of the physical findings were negative or normal. The patient's laboratory results are summarized in Table I. They were compatible with cirrhosis of the liver. In addition, the serum albumin was greatly diminished (2.9 Gm. per 100 ml.) and there was a leukopenia and thrombocytopenia. Evidence of renal disease was present. The alkaline phosphatase was increased, whereas the inorganic phosphorus was down to 2.7 mg. The patient had a high urine pH, uraturia, phosphaturia, and occasional tubular casts in the urine. An x-ray examination of the chest showed a mild rotary scoliosis and osteoporosis, as well as slight narrowing of the intravertebral The electroencephalogram was normal.

<sup>\*</sup>BAL, Hynson, Westcott & Dunning, Inc., Baltimore, Md.

TABLE I. COMPARISON OF SYMPTOMS AND LABORATORY RESULTS DURING TREATMENT AND PREGNANCY IN THE PATIENT WITH WILSON'S DISEASE

	UN- TREATED, SPRING, 1955	AFTER TREAT- MENT WITH CHELATING AGENTS, FALL, 1955	EXACERBA- TION, 1956	PREGNANCY		
				FIRST TRI- MESTER, SPRING, 1957	THIRD TRI- MESTER, FALL, 1957	3 MONTHS POST- PARTUM, EARLY 1958
Liver.—						
Enlargement	++	+	++	++	None	None
Anorexia, nausea	++	None	None	+	++++	None
Abdominal distress (right upper quadrant)	++	+	+	+++	++++	+
Serum bilirubin (mg.)	1.6	1.9		1.9	1.3	1.2
Bromsulphalein retention	21%		20%	14%	10%	20%
Prothrombin activity	40%	40%	50%		70%	85%
Cephalin flocculation	++++	++++	++++	++++	++++	++++
Alkaline phosphatase (units)	9.2		7.1		3	4.9
Kidney.—						
Albuminuria	+++	+	+++	++++	++++	+++‡
Amino-aciduria (cystinuria) Urine copper excretion	+++			++++†	++++†	++†
(per 24 hours)	1.8 mg.*			0.52  mg.	0.42 mg.	
Brain.—						
Tremor	++	+++	++++	+	+	+
Dysarthia	++++	+++	++++	+	+	+
Staggering gait	+	+	+++	+	None	None
Emotional overaction	+	++++	++	++++	++++	+

\*1950.

tCrystal formation.

‡With marked leukocytosis and moderate amount of bacteria.

During hospitalization the patient was placed on a low copper diet. She was treated with a chelating agent (Calcium Disodium Versenate) for 15 days. Thereafter it had to be discontinued because of marked side effects (headaches, nausea, abdominal discomfort, pruritus, and leukopenia). During the course of this medication her neurological symptoms grew worse.

A second course of Versenate was given one month later after which some improvement was noticeable, particularly of the liver disease. Immediately following this, the patient received another course of BAL. After five days, side effects appeared again and the treatment had to be discontinued. During that time her first pregnancy occurred. It ended at about 3 months in a missed abortion. During the removal of the missed abortion, the cul-de-sac was purposely punctured and a small amount of ascitic fluid was removed. In the fall of 1955 the patient appeared to be improved. Late in 1955 she again became pregnant. This pregnancy ended as an incomplete abortion at 2½ months with heavy blood loss. She happened to be Rh negative with a high Rh antibody titer. In view of the advanced Wilson's disease and expected Rh factor complications, the patient was advised against further pregnancies. Tubal ligation was recommended, but declined by the patient.

Though her physical improvement continued for more than one year, her mental condition deteriorated to a stage which necessitated commitment to a mental institution (Northville State Hospital). On admission to the mental institution the patient was again pregnant in the first trimester. A review of her menstrual history up to this point yielded the following significant data: she had her menarche at 17 years; her periods were irregular with prolonged intervals, dysmenorrhea, and heavy menorrhagia. They were misinterpreted as miscarriages on several occasions. At times they were associated with a flare-up of right upper quadrant abdominal distress, especially on postmenstrual days. A gynecological examination in 1955 revealed a hypoplastic uterus and tender adnexa.

The patient's last menstrual period was on Jan. 25, 1957. From that time on her brain syndrome became worse. The coarse tremor reappeared and she was more irritable, egocentric, and ambivalent. During the first weeks of pregnancy there was an extensive hyperemesis associated with nephrotoxic signs (albuminuria, tubular casts, puffiness of the face, and an increase in blood pressure). On one occasion she became febrile, confused, and was treated for impending hepatic coma. Spotty vaginal bleeding occurred. Fortunately there was no rise in the Rh antibody titer in this Rh-negative patient. Her husband was Rh positive of the heterozygous type. Thus it was assumed that the product of this conception was Rh negative and possibly not contributory to gestative complications. Later, the patient received luteal hormones which led to improvement during the latter part of this trimester. The control of her mental condition required promazine and Rauwolfia. Artane in moderate doses alleviated the tremor.

The patient continued to improve. The erythema of the palms (liver palms) began to fade, and the liver gradually diminished in size. The discomfort in the right upper quadrant of the abdomen disappeared. The prothrombin activity, blood count, alkaline phosphatase, and daily urine copper excretion became normal; the serum albumin rose. Tremor, dysarthia, and motor incoordination receded to a state in which she was able to do light work and to participate in social activities. She was given a leave of absence and encountered no great difficulties while she was away.

At about the beginning of the third trimester the patient returned to the hospital with abdominal cramps, inproportionate gain of weight, and a low-grade fever. The diastolic blood pressure was elevated (140/110) and she showed a marked albuminuria. Pus and bacteria were found abundantly in the urine. Fetal heart sounds were present and fetal movements were reported. Typical segmental arteriolar spasms were seen in the fundi of the patient's eyes. She was placed on a low sodium diet, and Rauwolfia was resumed. After a few days of bed rest the signs of impending toxemia faded away, except for albuminuria. In an attempt to consolidate the improvement, she was continued on the low sodium diet and Rauwolfia to the end of her pregnancy. Approximately 4 weeks before delivery the patient developed intense prodromal labor pains with uterine contractions. The cervix dilated and softened. The pains were more and more accompanied by vomiting and mental confusion the closer the day of confinement approached. They responded best to the administration of parenteral fluids (glucose, thiamine, and pyridoxine).

On the two-hundredth and ninety-seventh day labor began. In the first stage of labor, which lasted approximately 101/2 hours, the patient had weak, frequent, and irregular contractions with a very slowly effacing cervix. During these hours she was severely nauseated and vomited several times. Her temperature and blood pressure (140/115) rose. uterus failed to respond to oxytocics for about 10 hours of minimal progress. Then repeated administration of Pitocin succeeded in effectuating good contractions and almost immediate dilatation and retraction of the cervix. Under pudendal block the baby was delivered by outlet forceps from station plus 2, being in occipital anterior vertex position. The baby was a living boy who weighed 3,560 grams (7 pounds, 7% ounces). All signs of maturity were present and no developmental or pathological abnormalities were found. There was, however, less vernix caseosa covering the slightly macerated skin, and the subcutaneous turgor was diminished as seen in a stage of dehydration. The baby took large amounts of fluids avidly during his first hours of life. The placenta was delivered spontaneously 18 minutes later, weighed 620 grams, but was smaller than average in diameter. There were multiple medium-sized white infarcts. The blood loss during labor was estimated at 300 to 500 c.c. The total duration of the labor calculated from the rupture of the membranes to delivery of the baby was 10 hours and 45 minutes.

The patient had a normal immediate postpartum period and lying-in time. During the first 2 days after the delivery she was maintained on tetracycline. Rauwolfia medication was resumed thereafter. The psychiatrist and the social worker advised against breast feeding. The remission of Wilson's disease in this patient continued all through the 3 months' period of observation after the delivery. There was no flare-up of abdominal

distress and the postpartum involutional changes of the reproductive system took a regular course. Menstruation has not yet recurred. The formerly palpable liver has receded to normal size. Some of her liver function studies are again variably abnormal without seriously influencing her fair state of well-being. There is less evidence of kidney impairment. The Parkinsonism is still on the wane and permits her to participate in some activities and to attend to many of her needs. Emotionally, she seems to be more balanced, indicating a sustained and substantial remission.

#### Comments

This pregnant woman with Wilson's disease provokes several questions. First, what are the factors favorably contributing to the successful conception against the odds of advanced Wilson's disease? Second, what helped her to accomplish a full-term delivery, after the troublesome first trimester? Third, how can we explain the improvement? Fourth, what were the character and cause of the complications during late pregnancy? And, fifth, is it possible that her overterm pregnancy and uterine inertia had any relationship to her disease?

The identity of the Rh groups of mother and fetus precluded a lethal natural tendency of the fertilized egg and possibly a developmental interference. The patient's marriage was erotic, primitive, and impulsive, which may have played a preforming role for this pregnancy. She is from a family where eight or more children are the rule. A tendency toward fertility in our patient, therefore, would not be accidental.

In this case, pregnancy was discovered late in the first trimester. Hyperemesis and nephrotoxic signs may be interpreted to be of hepatic origin. Theoretically, complications during the first trimester would be uncommon, Drury and Bradbury could artificially induce ovulation and pseudopregnancy in estrous rats by injecting copper, provided the pituitary stalk was functionally intact. In our case we should assume a good estrogen level at the time of conception, and a promptly stimulating effect of the chorionic gonadotropin. Estrogen has also been found to increase the ceruloplasmin level and both these substances have their metabolic relations to the function of the liver.7 The point of the vicious imbalance in functions therefore might be directly related to a temporarily impaired estrogen and luteal hormone action after conception took place. From a different view, this case certainly demonstrates a close relationship of hyperemesis in pregnancy to disturbed liver function and possibly organic central nervous system defects. During the weeks of greatest distress in the first trimester of the pregnancy, our patient received vigorous supportive treatment of her liver impairment to which her improvement is related in time. It seemed as if this pregnancy could proceed in a normal manner after there was a reappearance of a fairly appropriate liver function.

The feature of this patient's pregnancy was the improvement in all spheres of her Wilson's disease. A fair interpretation would be to relate this improvement to the normalization of the copper metabolism. Our case shows several clues for it. During pregnancy there is an increasing demand for copper. Fetal tissues contain about five times as much copper as the average tissue. There is an increased retention of copper in the fetal circulation during the main phases of growth. Markovitz and co-workers<sup>6</sup> could provide evidence that non-ceruloplasmin copper approaches equilibrium with respect to diffusion across the placenta, whereas, concluded from studies of Scheinberg and co-workers,<sup>9, 10</sup> ceruloplasmin is unlikely to pass the placental barrier. The need for copper may suggest the return of the urine copper excretion to normal level.

Little is known about the copper intake and its resorption in the gastrointestinal tract. An alteration of the copper resorption in pregnancy could be the answer. An increased copper intake, however, may be excluded in our case since the woman's dietary habits remained the same. Also, Drury and Bradbury failed to raise the copper content of estrous rats by feeding them with a high copper diet.

Another possible factor in the patient's well-being during pregnancy might be changes in the ceruloplasmin levels. An increased ceruloplasmin level would absorb more copper, and thus bar it from being involved in the pathophysiology of this patient's primary disease. The literature is far from being unanimous about whether the ceruloplasmin level changes in pregnancy. Bearn¹ could demonstrate a fair correlation between the increase in ceruloplasmin and the bilirubin in the serum of patients with Wilson's disease. In our case this helps us to assume that the serum ceruloplasmin level remained constant, since the serum bilirubin level during pregnancy showed no significant alteration.

Analysis of the complications during the third trimester of the pregnancy in this case of Wilson's disease presents the following problems: emergence of nephropathy in pregnancy, early aggravated prodromal labor pains, uterine inertia during the first stage of parturition, and the complicated relations connected with overterm pregnancy. Pregnancies in patients with "Wilson's disease trait," i.e., in healthy siblings of patients suffering from Wilson's disease, were reported in several instances with toxemia. In our case of an advanced hepatolenticular degeneration, the symptoms of toxemia were somewhat variable apart from the typical ophthalmoscopic findings. The predominant observation was abdominal discomfort with nausea and marked albuminuria. Elevation in the blood pressure was mainly and significantly in the diastolic reading. Lack of edema formation points to a mechanism of fluid retention possibly different from that of the classical condition. The presence of a mild urinary tract infection slightly distorts the picture of a characteristic impending toxemia.

The distressing prodromal labor pains began at about the precalculated time of delivery. Together with the prolonged pregnancy and uterine inertia, they may be signs of a common etiology and apparently they have to do with the trigger mechanism of the labor. Fortunately, the patient's blood dyscrasia and impairment of the clotting mechanism improved to an optimum during the last week of pregnancy. The improvement continued during the lying-in period, lactation, and until the end of the time of observation. It enhanced the prospect of an uncomplicated determination of this pregnancy and encouraged us to adhere to a conservative management. Thus, this case again brought home the fact that nature will take care of herself in many instances, and that pregnancy is a decided blessing in more than one respect.

#### Summary

The occurrence and management of a pregnancy in advanced hepatolenticular degeneration have been described. The woman had previously been treated with chelating agents. During the eventful course of her illness, she had two early abortions. The reported pregnancy was accomplished 2 years later during the developing phase of an exacerbation.

Beginning in the latter part of the first trimester of this pregnancy there was an improvement in the Wilson's disease which continued through 3 months after parturition. The liver impairment receded to subclinical manifestations

and the secondary blood dyscrasia returned to an almost normal pattern. neurological symptoms-tremor, dysarthria, and motor incoordination-diminished greatly. The kidney impairment was reversed only to a minor degree. Daily urine copper excretion decreased to normal. Mental symptoms and the Kayser-Fleischer ring remained unchanged.

Symptoms of impending toxemia were observed at the end of the third trimester of the pregnancy. The pregnancy was carried beyond term and terminated in the spontaneous delivery of a healthy, normally developed baby. During the last 4 weeks before parturition there were unusually frequent severe prodromal pains and contractions. Uterine inertia was a feature of the labor.

Addendum.—Since this paper was submitted for publication we have carried on another year of observations and studies on this subject. After the woman's pregnancy, quarterly administrations of chelating agents delayed the progressive cirrhosis of the liver. Ceruloplasmin determinations revealed no such copper-binding fraction in her plasma. The infant, now nearly two years old, is developing at a healthy rate. His plasma ceruloplasmin level proved to be normal.

#### References

- Bearn, A. G.: Am. J. Med. 22: 747, 1957.
   Cartwright, G. E.: In McElroy, W. D., and Glass, B., editors: Copper Metabolism:

   A Symposium on Animal, Plant and Soil Relationships, Baltimore, 1950, Johns
- A Symposium on Animal, Plant and Soil Relationships, Baltimore, 1990, Johns Hopkins Press, p. 274.

  3. Cartwright, G. E., Hodges, R. E., Gubler, C. J., Mahoney, J. P., Daum, K., Wintrobe, M. M., and Bean, W. B.: J. Clin. Invest. 33: 1487, 1954.

  4. Drury, A., and Bradbury, J. T.: Am. J. Physiol. 139: 135, 1943.

  5. Glazebrook, A. J.: Edinburgh M. J. 52: 83, 1945.

  6. Markovitz, H., Gubler, C. J., Mahoney, J. P., Cartwright, G. E., and Wintrobe, M. M.:

  J. Clin. Invest. 34: 1498, 1955.

  7. Phys. E. M. and Raymund, J.: Proc. Soc. Exper. Biol. & Med. 92: 465, 1956.

- J. Chn. Invest. 34: 1498, 1955.
   Russ, E. M., and Raymund, J.: Proc. Soc. Exper. Biol. & Med. 92: 465, 1956.
   Scheinberg, I. H., and Gitlin, D.: Science 116: 484, 1952.
   Scheinberg, I. H., Cook, C. D., and Murphy, J. A.: J. Clin. Invest. 33: 963, 1954.
   Scheinberg, I. H., Dubin, D. T., and Harris, R. S.: J. Clin. Invest. 34: 961, 1955.
   Sullivan, F. L., Martin, H. L., and McDowell, F.: A. M. A. Arch. Neurol. & Psychiat. 69: 756, 1953.
   Hymn, J. J. Lyer, F. L. Chelmon, T. C. and Knewlton, M. Am. J. M. Sc. 231.
- 12. Uzman, L. L., Iber, F. L., Chalmers, T. C., and Knowlton, M.: Am. J. M. Sc. 231: 511, 1956.

# RUPTURED CEREBRAL ANEURYSM IN PREGNANCY AND PUERPERIUM

Report of 2 Cases

MAXWELL N. WACKER, M.D., CHICAGO, ILL.

(From the Departments of Obstetrics and Gynecology, The Chicago Medical School, Mount Sinai Hospital, and Edgewater Hospital)

THE maternal mortality is continuously being reduced below the so-called irreducible minimum. Death due to the common causes—hemorrhage, toxemia, and infection—is usually preventable.

Subarachnoid hemorrhage due to ruptured cerebral aneurysm is one example of a nonpreventable cause of maternal death. The dramatic fashion of the onset of symptoms plus the high mortality of the mother and baby make this cerebrovascular accident a challenge to the diagnostician.

The purpose of this paper is to review the literature briefly, to emphasize the diagnostic characteristics of subarachnoid hemorrhage, and to report 2 cases—one probable and one confirmed.

The term, "spontaneous subarachnoid hemorrhage," is descriptive of the clinical condition characterized by the sudden onset of severe headache followed shortly by nuchal rigidity, coma, and bloody spinal fluid. External physical trauma is excluded as an etiological factor. In the great majority of cases, the cause of the hemorrhage is rupture of an arterial aneurysm of the circle of Willis at the base of the brain.<sup>2, 7, 11</sup>

This paper will consider only ruptured cerebral aneurysm followed by subarachnoid hemorrhage; the 2 terms will be used interchangeably. I shall not discuss unruptured cerebral aneurysm or intracerebral hemorrhage which breaks into the subarachnoid space.

Many excellent monographs have been written on the subject of cerebral aneurysm<sup>2, 7, 11</sup>; however, it is not very often considered in obstetric publications. Pedowitz and Perell<sup>10</sup> recently reviewed the literature; 32 proved cases and 47 probable cases of cerebral aneurysm occurring during pregnancy and puerperium were included in the review. Since their paper was published there have been other case reports.<sup>1, 5</sup>

Case 1.—A 34-year-old white woman, gravida ii, para i, was seen on Dec. 24, 1949, with a history of amenorrhea since Oct. 30, 1949.

Her past medical, surgical, and family history was unimportant. Her previous pregnancy and delivery were normal. The physical examination revealed no abnormal findings; the uterus was enlarged to the size of a 10 weeks' gestation. The blood pressure was 104/70. The laboratory findings were all within normal limits.

The subsequent prenatal course was uneventful and included 11 office visits; the blood pressure varied between 110/70 and 120/80.

Labor began spontaneously one week prior to term on July 16, 1950, at 2:30 P.M. The patient was admitted to Edgewater Hospital and at 3:30 P.M. she was delivered spontaneously of a living male baby weighing 5 pounds.

The puerperium was uneventful until the seventh day post partum. At 11:30 P.M. she complained of a sudden, severe headache. One-half hour later examination revealed the patient to be semicomatose. Nuchal rigidity was present. The blood pressure was 190/98. At 3:00 A.M. generalized tremors developed. Treatment included the administration of oxygen, 2 c.c. of 50 per cent solution of magnesium sulfate, and 500 c.c. of 25 per cent solution of dextrose intravenously. Phenobarbital, 3 grains, was given intramuscularly. Neurologic consultation was obtained.

Spinal puncture revealed bloody spinal fluid under increased pressure. The patient remained in deep coma. A second spinal tap done 24 hours after the first was also bloody. At this time urinalysis showed 4 plus proteinuria and 2 plus glycosuria. The blood pressure was now 120/70.

The condition of the patient became steadily worse; the temperature rose to 104° F. rectally, the blood pressure dropped to 80/0, and death occurred at 10:35 p.m., July 25, 1950, 9 days post partum and approximately 48 hours after the onset of headache.

Permission for autopsy could not be obtained. The diagnosis was spontaneous sub-arachnoid hemorrhage due to rupture of cerebral aneurysm.

Case 2.—A 24-year-old white woman, gravida i, para 0, was admitted to Mount Sinai Hospital at 9:00 p.m., July 24, 1957, complaining of severe headache and blurred vision. The last normal menses occurred Nov. 16, 1956; the duration of gestation was 36 weeks.

At the age of 18 the patient had been found to have a blood pressure of 200/100. Since then she had been under continuous medical supervision. In 1954, at the age of 21, she had been hospitalized because of blurring of vision in the left eye. Slight choking of the disc and retinal hemorrhage were found in the left eye. The results of complete blood chemistry studies and urinalysis were within normal limits. The blood pressure was 150/100.

The patient was referred to me by the internist as soon as he discovered she was pregnant. On Jan. 19, 1957, the blood pressure was 170/90. Physical examination did not reveal any abnormalities. Vaginal examination confirmed the presence of an 8 to 10 weeks' pregnancy. The pelvic measurements were normal. The routine laboratory tests and chemical studies of the blood revealed normal values.

The prenatal course for the following 7 months was uneventful. The blood pressure ranged between 180 and 160 systolic and between 100 and 90 diastolic. The urine remained normal; the patient's weight increased by 8 pounds. Except for occasional headaches she had no complaints.

On July 24, 1957, at 36 weeks' gestation, the patient notified me that she had had a constant severe headache all day with some blurring of vision. She was admitted to the hospital at 9:00 P.M. of the same day.

On admission she did not appear to be acutely ill. Her chief complaint was severe constant headache and blurred vision. The blood pressure was 170/110. Funduscopic examination revealed moderate choked discs and recent hemorrhages in the right retina. The uterus was enlarged to the size of a 36 weeks' gestation; the presentation was cephalic and the fetal heart sounds were normal. A diagnosis was made of pregnancy complicated by essential hypertension with superimposed toxemia.

The immediate treatment was rest in bed; icecap applied to the head; Demerol, 75 mg., and phenobarbital, 100 mg., given intramuscularly. About 30 minutes after admission the patient began to complain bitterly of pain in the left eye. She became very restless and began to scream. Two hours later she became comatose. Her skin was cold, pale, and sweaty; the respirations were irregular and gasping. The blood pressure was 250/130.

10

1e

of

nf.

y.

nt

re

F.

0,

b-

ai n.

0.

of od od.

ii.

re

ed he

he

re

ie

a.

lie

ed

g.,

he

nd

nd

The patient was placed in an oxygen tent. An infusion of 50 per cent dextrose in water was started and 2 c.c. of a 50 per cent solution of magnesium sulfate was given intramuscularly. Neurologic examination revealed nuchal rigidity and hyperactive reflexes in all extremities. Multiple retinal hemorrhages and choked discs were seen bilaterally.

For the next 12 hours the patient remained more or less in a coma. There were short periods of consciousness during which she complained of headache. The blood pressure dropped to 140/110; the pulse became strong and slow, with a rate of 72 per minute. At 11:40 A.M. on July 25, 1957, about 14 hours after admission, the patient had a generalized convulsion, became deeply cyanotic, and died 20 minutes after the onset of the convulsion.

Preparations had been made for cesarean section when it was apparent that the mother was in extremis. The moment her heart sounds ceased, the abdomen and uterus were incised and a living female baby was delivered. The infant was immediately taken to the premature nursery. The birth weight was 4 pounds, 11 ounces. The baby thrived and was discharged from the hospital at 4 weeks of age weighing 5 pounds, 11 ounces, in apparently normal condition.

Autopsy findings of the mother included ruptured aneurysm of the circle of Willis at the bifurcation of the basilar artery. The left adrenal was replaced by a large pear-shaped mass which was attached to and involved the paravertebral sympathetic ganglia from T-3 to T-10.

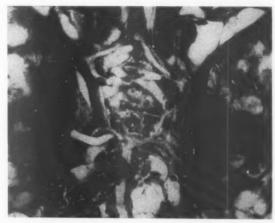


Fig. 1.—Case 2. Ruptured aneurysm at the bifurcation of the basilar artery.

The diagnosis was ruptured berry aneurysm (Fig. 1) of the circle of Willis, subarachnoid hemorrhage, ganglioneurofibromatosis of thoracic sympathetic chain, and ganglioneuroma of left adrenal.

#### Comment

These 2 cases are representative of 2 major groups of patients with ruptured cerebral aneurysm. In Case 1, the patient was apparently normal in every respect; subarachnoid hemorrhage was like a bolt from the blue. Approximately 40 per cent of patients in this group have no antecedent disease or complaints. In about 25 per cent of reported cases rupture of the cerebral aneurysm occurred during labor or shortly after delivery. In this case (Case 1) the cerebral aneurysm withstood the increased pressure of labor only to rupture on the seventh postpartum day.

Case 2 is typical of a large group of patients comprising about 20 per cent of one series.<sup>7</sup> These patients were hypertensive prior to the rupture of the cerebral aneurysm. In the second case it is likely that a hypertensive crisis occurred causing the aneurysm to rupture its wall.

Pathogenesis.—The aneurysm develops because of a congenital weakness of the wall of the vessels of the circle of Willis. True congenital cerebral aneurysms have been reported in several newborns. Usually the aneurysm occurs at a bifurcation of the vessel. The size of the aneurysm is often small, varying from 4 to 10 mm. At autopsy skillful dissection is usually necessary to locate the site of the blowout.

What causes the aneurysm to burst? The rupture of a cerebral aneurysm is contingent on such vagaries as its age, size, and location. It is logical to assume that physical stresses and strains which tend to raise the pressure of the blood in the cerebral vessels should predispose to rupture. However, ruptures occur in the second trimester, with its midgestational drop in blood pressure, almost as often as they occur during labor, when presumably the stress is greater. Most ruptures occur in the third trimester.<sup>10</sup>

About 80 per cent of diagnosed unruptured aneurysms eventually rupture.<sup>7</sup> Approximately 50 per cent of patients with ruptured aneurysm die shortly after the first attack<sup>11</sup>; the second rupture usually occurs 2 to 4 weeks after the first and kills 75 per cent of the remaining patients. The operative mortality of

brain surgery for cerebral aneurysm is 50 per cent.

Treatment.—It is obvious on the basis of mortality statistics that not much can be done for the mother after subarachnoid hemorrhage has occurred. Symptomatic treatment including spinal puncture is generally advocated. If the patient survives the first attack, angiograms and arteriograms may be made to localize the lesion in the brain and to determine the operability.<sup>1, 4</sup>

When the fetus is viable the best method of delivery is often debatable. Spontaneous delivery<sup>6</sup> is advocated as often as cesarean section.<sup>3</sup> It is regret-

table that often the mother dies undelivered.

The fetus deserving the most consideration is the one at or near term. Rarely are the circumstances propitious for a rapid forceps delivery prior to the death of the mother. Reliance for the rescue of the baby from the dying mother must be placed on cesarean section. This is usually performed immediately after the death of the mother.

Failure of the baby to survive is probably due to the progressive anoxemia. Continuous administration of oxygen to the dying mother may help to maintain adequate oxygen tension in the circulation. In addition to the maturity of the fetus, the prognosis for the baby seems also dependent on how quickly it can be

removed from the uterus after the death of the mother.

Postmortem Cesarean Section.—The pros and cons of this operation have been outlined adequately in the literature,<sup>8, 12</sup> including the legal and moral issues. The survival rate of babies delivered by postmortem cesarean section is extremely low. At Mount Sinai Hospital the records of the last 42 years include

9 postmortem cesarean sections; none of the 9 babies survived.

The following factors may have contributed to the survival of the baby in Case 2: (1) the advanced gestational age of the fetus—36 weeks (most of the neonatal deaths have been associated with prematurity); (2) the continuous administration of oxygen to the mother; (3) the rapid course of the illness; (4) the prompt removal of the fetus from the uterus before severe hypoxia caused irreversible brain damage.

#### Summary and Conclusion

Spontaneous subarachnoid hemorrhage is nearly always due to rupture of a cerebral aneurysm. The clinical and pathologic characteristics were discussed. Pregnancy does not seem to alter these characteristics. Prompt diagnosis may prolong the life of the mother and the fetus though the mortality is very high.

1ec.

188

lis\*

m 11,

to

sm

to

he

'es e, is

e.7

er

st

of

ch d. If de le. etm. to ng mia. in he be

ve al is de in he us SS: ia

of ed. ay h.

Two cases were discussed. In one, a postmortem cesarean section resulted in a normal baby which survived.

I wish to express my appreciation for the assistance of Dr. H. T. Grinvalsky, Department of Pathology, Mount Sinai Hospital, Chicago, Ill.

#### References

- Bleakney, R.: South. M. J. 50: 1168, 1957.
   Brain, W. R.: Diseases of the Nervous System, ed. 4, New York, 1951, Oxford University
- Press.
  3. Conley, J. W., and Rand, C. W.: A. M. A. Arch. Neurol. & Psychiat. 66: 443, 1951.
  4. Feldman, R. L., Gross, S. W., and Wimpfheimer, S.: Am. J. Obst. & Gynec. 70: 289,
- 5. Finola, G. C.: Am. J. OBST. & GYNEC. 74: 1342, 1957.
- 6. Fleming, S. P., and Mauzy, C. H.: Am. J. Obst. & Gynec. 70: 1133, 1955.
  7. Hamby, W. B.: Intracranial Aneurysm, Springfield, Ill., 1952, Charles C Thomas, Pub-7. Hamby, lisher.

- 8. Lattuada, H. P.: Am. J. Surg. 84: 212, 1952. 9. Newcomb, A. L., and Munns, G. F.: Pediatrics 3: 769, 1949. 10. Pedowitz, P., and Perell, A.: Am. J. Obst. & Gynec. 73: 736, 1957. 11. Richardson, J. C., and Hyland, H. H.: Medicine 20: 1, 1941. 12. Weil, A. M., and Graber, V. R.: Am. J. Obst. & Gynec. 73: 754, 1957.

# MATERNAL DEATH RESULTING FROM ACUTE GASTRIC HEMORRHAGE DUE TO SCHISTOSOMA MANSONI

Report of a Case

Albert J. Kahane, Captain, USAF (MC)\* and Francisco B. Martin, M.D., Brooklyn, N. Y.

(From the Department of Obstetrics and Gynecology and Department of Pathology, The Long Island College Hospital, and the State University of New York, College of Medicine at New York City)

WITH the recent large influx of Puerto Ricans into the continental United States, the problem of parasitic infestation is becoming a very real one. It is presently estimated that there are over 700,000 Puerto Ricans in New York City alone.<sup>2</sup> Various investigators feel that from 15 to 25 per cent of this population harbors parasites.<sup>2</sup> Thus in this city there may be assumed to be over 150,000 cases. In the case of Schistosoma mansoni it is estimated that 20 to 25 per cent of the Puerto Rican population is infested with this parasite, which is the commonest blood fluke of man found in the Western Hemisphere.<sup>6</sup> It occurs more frequently in adolescents and in those under 21 years of age. Therefore in this population where early marriage is not uncommon, this and other parasites may first be detected during pregnancy when prenatal care is sought. The following is believed to be the first maternal death due to infestation with this parasite reported in American literature.

Mrs. A. M., a 25-year-old Puerto Rican woman, para 0-0-1-0, was first seen in the Obstetrical Clinic of The Long Island College Hospital on July 10, 1957, in the twentieth week of gestation. The last reported menstrual period was Feb. 20, 1957, and the expected date of confinement was Nov. 27, 1957. Past history was essentially negative except for a complete spontaneous abortion at 6 weeks' gestation in 1956. She had been married 1½ years and had come to New York from Puerto Rico 2 years previously. At this first clinic visit, a Grade I precordial systolic murmur was noted. Her blood pressure was 120/80, her weight was 125¼ pounds, and her height, 5 feet, 1 inch. Routine laboratory data were as follows: Urine specific gravity 1.015; hemoglobin, 13 Gm.; white blood count, 10,850, 75 polymorphonuclear neutrophil leukocytes, 15 lymphocytes, 6 monocytes, 4 eosinophils; VDRL test, negative.

The pregnancy was uneventful until Oct. 24, 1957, when, in the thirty-fifth week of gestation, the patient started to show early toxemic signs of weight gain, hypertension, and albuminuria. In spite of diuretics and a low salt diet there was no improvement. On Nov. 6, 1957, the weight was 142 pounds and the blood pressure 130/98. The patient was admitted to the Obstetrical Service because of mild pre-eclampsia. (There was no obvious edema but the patient was unable to remove her wedding band.)

<sup>\*</sup>The contents reflect the personal views of the authors and are not to be construed as representing a statement of official Air Force policy.

ND

ng

w

d

e.

f

d

d

1-

S

3-

h

e

h

Ç-

e

n

t

e

d

4

At the time of admission the blood pressure was 170/100 and during the first 5 days of hospitalization, the systolic pressure fluctuated between 120 and 140 and the diastolic between 80 and 95. Daily urinalysis for albumin was persistently 1 plus. Intake and output balanced well. An ophthalmological consultant found no retinal changes. A routine medical consultation at that time recorded a normal past history, but the patient admitted to a moderately heavy alcoholic intake. A blowing Grade II systolic murmur was heard at the apex. The heart was not enlarged, and the rhythm was regular. The liver, kidneys, and spleen were not palpable. Laboratory results upon admission were: red blood count, 4.4; hemoglobin, 12.8 Gm., white blood count, 9,500; polymorphonuclear neutrophil leukocytes, 74; lymphocytes, 11; eosinophils, 15; hematocrit, 38; blood urea nitrogen, 6.5; and uric acid, 4.0. All other studies were within normal range. In view of the eosinophilia on admission, stools were tested for ova and parasites and revealed hookworm and Trichuris ova.

On Nov. 12, 1957, 6 days after admission, in spite of bed rest, diuretics, and a low salt diet, the patient's condition was deteriorating as was evidenced by increasing urinary albumin from 1 plus to 2 to 3 plus, and hypertension of 140/100. The estimated fetal weight was 2,400 grams and it was advised that cesarean section be performed in the interests of both the mother and the infant. Accordingly, on Nov. 12, 1957, the patient was delivered by low flap cesarean section under spinal anesthesia of a 2,470 gram male infant of good color and with a good cry. Both mother and child left the operating room in good condition. At the time of the operation, the abdomen was explored, and the liver was noted to be "nodular and firm, having the consistency of a cirrhotic type of liver." In view of this, a liver study was performed 2 days postoperatively (Nov. 14, 1957) and revealed an alkaline phosphatase of 4.8; bromsulphalein, 14 per cent; and cephalin floculation, 1 plus.

Postoperatively, the daily blood pressure varied from 120/80 to 125/95. The patient's postoperative course was essentially uneventful until Nov. 19, 1957, when, at 11:00 p.m., she felt dizzy and vomited approximately 300 c.c. of bright red blood with clots. She was placed in bed and had a series of tonic and clonic convulsions of approximately 30 to 45 seconds' duration accompanied by tongue biting and an upward gaze. The blood pressure was 110/90 and the urine showed a trace of albumin. The patient's condition was stable through the night, but on Nov. 20, 1957, at 8:00 a.m., there was another episode of massive bright red hematemesis and a large tarry stool mixed with bright red blood was passed. The blood pressure dropped to 70/40. The sclerae were not icteric, but dilated venules were noted at the base of the tongue and buccal mucosa. The lungs were clear. The liver edge was palpable about 3 to 4 cm. below the right costal margin.

A Sengstaken-Blakemore tube was passed while the patient continued to vomit large amounts of bright red blood. Transfusions were started but the blood pressure dropped to 0 and then returned slowly. After passage of the tube, the bleeding subsided and the blood pressure was maintained at 110 to 120/70 but the tube continued to drain dark, bloody fluid. Transfusions of whole blood, intravenous glucose, tetracycline, and vitamin K were administered. The drainage from the stomach became light, bile-colored and the patient became slightly icteric. At 7:00 p.m. on Nov. 20, 1957, the bright red bleeding again started, but this time it was uncontrollable and, in spite of blood replacement, sedation, and calcium gluconate intravenously, the patient died at 8:00 p.m., approximately 21 hours after the initial episode.

Postmortem examination revealed a well-developed, well-nourished Puerto Rican woman. Positive findings were as follows:

The heart weighed 350 grams and appeared slightly enlarged with preponderance of the right ventricle. The right atrium showed moderate dilatation. The wall of the right ventricle showed moderate hypertrophy. The papillary muscles and trabeculae carneae appeared thick and prominent. The left ventricle showed moderate hypertrophy and dilatation. Sections of the myocardium showed no abnormalities in color or consistency. The valves and coronary arteries were unremarkable.

Together the lungs weighed 560 grams. They were slightly rubbery in consistency; the external surfaces had a grayish-blue smooth appearance, and no nodules could be felt.

of

ar

On section, the cut surface showed a markedly congested parenchyma. The tracheobronchial tree was not remarkable. The main branches of the pulmonary artery showed an intima which contained several yellowish, nonelevated areas scattered throughout.

The liver weighed 1,750 grams and was very firm in consistency. It showed a diffuse whitish thickened capsule and marked coarse lobulations of the external surface. On section, the cut surface showed distinct grayish-white zones surrounding the portal spaces, these varied in size being widest around the largest portal spaces near the hilus and becoming progressively small toward the periphery (Fig. 1).

The spleen weighed 250 grams. The capsule appeared wrinkled and cut section showed small distinct follicles and prominent trabecular markings. The kidneys weighed 420 grams together. They showed smooth, pale external surfaces. On section, the corticomedulary junctions were well demarcated and the medullary portions appeared markedly congested.

The esophagus showed two small areas of mucosal ulceration, 4 and 7 cm. proximal to the cardia, but no varices could be demonstrated. The stomach contained 300 c.c. of dark bloody material. The lining mucosa was well preserved with prominent rugae. In the posterior wall and 3 cm. distal to the cardia there was a small rounded area of ulceration measuring 0.6 cm. in diameter and having nonelevated borders and a hemorrhagic base.



Fig. 1.-Cut surface of liver showing coarse lobulation and thickened capsule,

On microscopic examination, it was seen the sections of the lungs contained numerous miliary granulomatous lesions (pseudotubercles) showing epithelioid and histiocytic cellular reaction with lymphocytic and plasma cell infiltration, especially around the margins of the nodules. Some of the nodules contained remnants of ova, sometimes with foreign body giant cell reaction (Fig. 2). Some pulmonary vessels showed occlusion of their lumina by proliferating well-vascularized connective tissue. Other sections of lung showed fibrous thickening of alveolar septa and filling of air spaces by neutrophils and macrophages with fibrinous exudate and a focus of necrosis of parenchyma.

The spleen showed diffuse fibrosis. The liver parenchyma was subdivided into pseudolobules by ramifying trabeculae of fibrous tissue. These sometimes contained proliferating bile ducts and foci of lymphocytic and plasma cell infiltration. Granulomatous nodules were also encountered showing foreign body giant cell reaction around parasitic ova of Schistosoma (Fig. 3). Some of the nodules were in the hepatic parenchyma.

The kidney glomeruli showed slight increase in cellularity and thickening of the basement membranes.

en-

ed

se

On

es,

on

ed

0.

ly

of In a-

ic

th

ıg

d

0

0.

ic

Multiple sections of the small and large bowel showed only 3 small foci of fibrosis deep in the mucosa and sometimes within the muscularis mucosa. These were comprised of dense collagenous tissue with calcified remnants of ova in their central portion. The area of ulceration grossly noted in the stomach microscopically showed superficial ulceration with a partially necrotic and thrombosed vein at its base. The vein was unusually large for this location and constituted a varix. The esophagus showed superficial erosions with local accumulations of neutrophils, but no varices in the submucosa.

The final anatomical diagnoses were: (1) schistosomiasis with lesions involving the liver, kidneys, and lung; (2) cirrhosis of the liver due to Schistosoma mansoni; (3) dilatation (varix) with secondary rupture of the vein in upper portion of stomach; (4) massive gastrointestinal hemorrhage secondary to ruptured gastric varix; (5) endoarteritis of the pulmonary vessels due to schistosomiasis; (6) hypertrophy of the right side of heart; (7) mild proliferative glomerulitis.

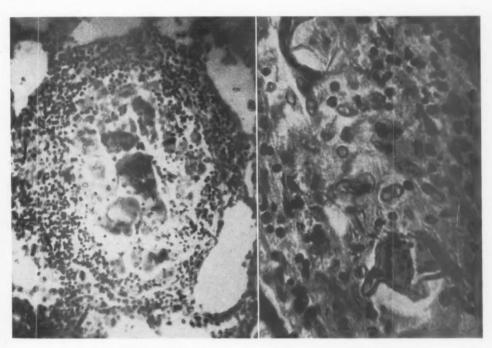


Fig. 2

Fig. 3.

Fig. 2.—Section of lung pseudotubercle with ova and giant cell reaction.

Fig. 3.—Granulomatous liver nodule with foreign body giant cell reaction about parasitic

# Comments

It is interesting to note in this case the paucity of clinical symptoms prior to the fatal hemorrhage and the findings at postmortem. There was no antecedent history compatible with either chronic lung disease or cardiac disease, which may be assumed to have existed for a considerable length of time to result in the findings noted at autopsy.

In spite of the severe involvement of the pulmonary parenchyma by the granulomatous lesions and the endarteritic changes present in the small pulmonary vessels which probably resulted in pulmonary hypertension as evidenced by right-sided cardiac hypertrophy, no clinical symptoms existed nor

were any gross lesions evident at autopsy. (However, Shaw and Ghareeb, as well as Rodriquez,5 state that in 80 per cent of cases of parenchymatous lesions no gross changes are visible.)

Another point of note is that repeated stool examinations, though positive for Trichuris and hookworm ova, were negative for S. mansoni. This was confirmed by the absence of living parasites of S. mansoni in the gastrointestinal tract at postmortem examination. Evidence of old infestation was manifested by the presence of old fibrotic nodules associated with calcified ova found in multiple sections of the small bowel. (Multiple infestation with parasites is the rule rather than the exception.)

The cirrhosis of the liver was of the classical "pipestem" type, which resulted in portal hypertension with compensatory collateral circulation and venous dilatation of the cardiac veins of the stomach which ultimately caused the fatal gastric hemorrhage. However, the lower esophagus failed to show varices.

It should be pointed out that when lesions of the gastrointestinal tract are found, the lungs and liver should be thoroughly investigated and vice versa because the infestation has multiple foci. Also, the parasites may not be found in any abundance but the parenchymatous changes may be extensive.

Clinically the patient had toxemia of pregnancy as shown by hypertension and albuminuria with weight gain. However, the only postmortem finding compatible with this clinical impression was a mild proliferating glomerulitis.

It has been shown that in massive infections with S. mansoni, amazingly few gastrointestinal symptoms may be encountered, but the disease may be widely disseminated even in the absence of symptoms. Authors also state that the manifestations of the disease are dependent upon the intensity and frequency of exposure to infection.1, 3, 4, 6, 7

Along with the first episode of hematemesis there was an associated convulsion but the brain was not autopsied and consequently the reason for this remains unknown.

In passing it may be pointed out that the exploration of the abdominal viscera at the time of laparotomy (for any purpose) may be the first indication of a silent but possibly very serious pre-existing disease, and should be standard procedure whenever feasible.

# Summary

A maternal mortality resulting from acute gastric hemorrhage due to S. mansoni has been described. The authors feel that with the increasing influx of Central and South Americans into the continental United States, parasitie infestation is a real public health problem affecting all of the medical specialties and it must be recognized as such.

We wish to express our deep appreciation to Miss Frances Beynon for her assistance and cooperation in the preparation of this paper.

#### References

- 1. Ash, J. E., and Spitz, S.: Pathology of Tropical Diseases, Philadelphia, 1945, W. B.
- Saunders Company, p. 274.

  2. Friedman, E. A., and Shookhoff, H. B.: New York J. Med. 57: 3994, 1957.

  3. Koppisch, E.: In Anderson, W. A. D., editor: Pathology, ed. 2, St. Louis, 1953, The C. V. Mosby Company, p. 384.
- 4. Pons, A. P.: Tratado de enfermadades infecciosas, Barcelona, Spain, 1950, Salvat Edi-
- Fons, A. F.: Tratado de enfermadades infecciosas, Barcelona, Spain, 1950, Salvat Editores, S. A., vol. 6, p. 752.
   Rodriquez, H. F., and Rivera, E.: New England J. Med. 258: 1196, 1958.
   Rodriquez-Molina, R.: In Harrison, T. R., et al., editors: Principles of Internal Medicine, ed. 2, New York, 1954, Blakiston Company, p. 1167.
   Shaw, A. E., and Ghareeb, A. A.: J. Path. & Bact. 46: 401, 1938.

# NORMAL PREGNANCIES IN A JUVENILE HYPOTHYROID PATIENT

d

n

d

t

t

n

g

t

-

S

Julio Paz-Carranza, M.D.,\* Martin Perlmutter, M.D., and Lowel Prigerson, M.D., Brooklyn, N. Y.

(From the Department of Medical Services, Maimonides Hospital of Brooklyn and the Department of Medicine, State University of New York College of Medicine at New York City)

SURVIVAL of children with hypothyroidism, congenital or acquired, until the childbearing age is not unusual. A successful pregnancy in such an individual, however, is unusual, if she has not received thyroid replacement therapy. We have been able to find in the literature reports of pregnancies occurring in 6 untreated cretins. In 1897, Townsend¹ presented a case of a typical cretin who became pregnant; no mention of therapy was made in this report. Five years later, Herrgott² reported a pregnancy in a juvenile hypothyroid patient; once again this article did not mention therapy. Burk and Kerr³ referred to Merguet's cretinous patient who became pregnant without any thyroid hormone treatment. In 1943, in a review of the subject, Parkin and Greene⁴ reported the coincidence of pregnancy and hypothyroidism in one juvenile hypothyroid patient and in one cretin. Finally, Zondek,⁵ in the fourth edition of his "Diseases of the Endocrine Glands," mentioned another untreated cretin who became pregnant.

The purpose of this report is to record the observations of a patient who was delivered of two normal children despite untreated prepubertal hypothyroidism and who subsequently developed the typical picture of severe myxedema.

### Case Report

A. L. (M.H. No. 27643), a 30-year-old Puerto Rican housewife, was admitted to the Maimonides Hospital of Brooklyn on Dec. 12, 1957, because of progressive sleepiness and fatigue of 8 months' duration. Mental development in her early childhood appeared to have been normal except that her growth seemed to have been somewhat retarded, since she was the shortest of her 12 siblings. Her schooling consisted of five grades in the Puerto Rican public schools, where she learned to read and write. The time of menarche is unknown as are details of her menstrual history. After 3 years of infertile married life, she became pregnant at the age of 23 without the aid of medication. Within 2 years she had two live normal children, each delivered by cesarean section. At the time of the second cesarean section, she believes that the tubes were ligated to prevent future pregnancies.

The 5 years following her second pregnancy were marked by an increasingly heavy menstrual flow. For about 8 months prior to admission, she noted the gradual onset of

Present address: 12 Ave. 1-55, Zona 2, Guatemala City, Guatemala.

swelling of the face, increasing fatigability, and lethargy. The hands and feet were swollen. Cold intolerance and constipation were quite severe. Shortly before hospitalization, dyspnea and a sensation of tightness across the chest would develop after walking two to three blocks.

Physical examination revealed a small, lethargic woman who looked like a cretin. Her height was 4 feet, 5 inches, her weight 95 pounds. She answered questions in a slow, deliberate, hoarse voice. The pulse was 80 per minute. The blood pressure 110/70 and the respirations 20 per minute. The skin was pale, coarse, dry, and scaly. The hair of the scalp was scanty and coarse. There was no axillary hair and the pubic hair was sparse. The tongue was enlarged. The thyroid gland was not palpable. The heart appeared questionably



Fig. 1.—Appearance of patient prior to therapy.

enlarged to the left; the sounds were normal. There was a lower abdominal midline surgical scar. The extremities and fingers were small. Although the hands and feet were puffy, there was no pitting edema.

Routine laboratory examination disclosed a marked anemia. The hemoglobin varied between 5.4 and 7.9 Gm. per 100 ml., and there were 2.9 million red cells per cubic centimeter of blood. The blood smear showed hypochromia, anisocytosis, and polychromatophilia. The mean corpuscular hemoglobin concentration was 27.6 per cent, the mean corpuscular volume was 85.5 cubic microns, and the mean corpuscular hemoglobin was 25.6 micromicrograms. There was a moderate eosinophilia, presumably associated with the presence of ova of both

n.

18

S.

ap.

e-

le

163

Trichuris trichiura and Necator americanus in the stool. Blood serological tests for syphilis were repeatedly positive but the serological test and colloidal gold curve of the spinal fluid were normal. The fasting blood sugar, urea nitrogen, and serum electrolytes were normal.

Endocrinological studies demonstrated that the thyroid gland was not functioning: the thyroidal uptake of radioactive iodine at 24 hours was 2 per cent (normal range 15-50 per cent); the serum protein-bound iodine was 1.3 gamma per cent (normal range 3-7 gamma per cent); the serum cholesterol was 314 mg. per cent. The urinary excretion of 17-hydroxycorticoids was 1.7 mg. per day (normal 3-9 mg.); the urinary gonadotropin assay was slightly positive for 7 mouse units and negative for 63 mouse units.

Roentgen examinations of the bones showed incomplete fusion of the epiphyses of the acetabula, hips, knees, feet, elbows, wrists, and hands. The epiphyses of the vertebral bodies were small and the corners of these vertebral bodies were deficient. Vascular channels were visible in some of the dorsal vertebrae. The sella turcica was of normal size. The generalized delayed epiphyseal fusion was interpreted by Dr. E. Levin as compatible with juvenile hypothyroidism. There was no deformity or fragmentation of epiphyseal centers, however, as is characteristically seen in childhood cretinism.

Cardiovascular studies revealed a venous pressure of 160 mm, of water. The circulation time was 14 seconds despite the marked anemia. At x-ray examination, the size of the heart was large in relation to a small chest cage. The size and shape of the heart were compatible with the diagnosis of pericardial effusion. The electrocardiogram showed low T waves which were considered consistent with, but not diagnostic of, myxedema.

After the initial laboratory studies were completed, the patient was given 1 mg. of tetra-iodothyroacetic acid (Tetrac\*) per day for one week, followed by 2 mg. daily for 6 days. On the fourth day of ingestion of this thyroxine analogue there was noted the onset of improvement which led in 2 weeks to moderate clinical improvement in mental alertness, facial appearance, and physical vigor. After the second week of Tetrac therapy, the patient received 60 mg, of desiccated thyroid per day. She has been lost from follow-up care. The two children of the patient were examined and appeared to be normal. The uptake of I131 by their thyroid glands at 24 hours was 30 and 38 per cent, respectively.

#### Comment and Summary

It is of interest to note that this patient who had evidence of previously untreated hypothyroidism which antedated her puberty, was able not only to conceive, but to carry to term, two normal children. The patient's short stature and the incomplete epiphyseal fusion at the age of 30 indicate that she was moderately hypothyroid during the prepuberal period. About 4 years after the delivery of her second child she developed symptoms of severe myxedema. Indeed, the combination of the dwarfism and severe myxedema gave her the appearance of an untreated cretin.

Another case of normal pregnancy in a patient who had had untreated juvenile hypothyroidism is presented.

The endocrinological tests were performed at the Endocrine Laboratory of the Maimonides Hospital by Mr. Marvin Numeroff, Chemist, to whom we are greatly indebted.

### References

- Townsend, C. W.: Arch. Pediat. 14: 20, 1897.
   Herrgott, A.: Ann. de gynec. 58: 1, 1902.

- Herrgott, A.: Ann. te gynec. 38. 1, 1902.
   Burk, K., and Kerr, A., Jr.: Am. J. Obst. & Gynec. 68: 1623, 1954.
   Parkin, G., and Greene, J. A.: J. Clin. Endocrinol. 3: 466, 1943.
   Zondek, H.: The Diseases of the Endocrine Glands, ed. 4 (second English edition), Baltimore, 1944, Williams & Wilkins Company, p. 207.

<sup>\*</sup>Supplied by the Warner-Chilcott Laboratories, Morris Plains, N. J.

# PREGNANCY IN A NONCOMMUNICATING RUDIMENTARY HORN\*

Report of a Case

ELMER GERGELY, M.D., AND DANIEL J. MASON, M.D.,\*\*
BROOKLYN, N. Y.

(From the State University of New York, College of Medicine at New York City, and the Department of Obstetrics and Gynecology at Maimonides Hospital)

THE obstetrical literature has numerous reports concerning the association of malformation of the female genital tract and pregnancy. The complications arising from pregnancies in anomalous uteri are rarely diagnosed. This communication reports a case in which a pregnancy occurred in a non-communicating rudimentary horn of a uterus bicornis unicollis.

#### Review

Uterine anomalies can be responsible for many complications that may occur during pregnancy, labor, or puerperium. It is, therefore, essential to make the diagnosis of a congenital uterine anomaly early in pregnancy. The uterus didelphys and the more common uterus bicornis offer no diagnostic problem if a thorough vaginal and speculum examination has been done. In those patients with a history of sterility, repeated abortions, recurrent premature labors, or abnormal presentations, hysterosalpingography should be performed. Jarcho, Fenton and Singh, and Baker have shown that between 18 and 53 per cent of pregnancies associated with uterine anomalies will spontaneously abort, and between 13 and 15 per cent will go into premature labor. Between 10 and 30 per cent will have a malpresentation such as a breech or a transverse lie with the latter occurring more frequently in the uterus subseptus and uterus bicornis unicollis than in other types of anomalies. During labor there is the possibility of uterine rupture but this rarely occurs. A nonpregnant horn may become incarcerated and cause failure of descent by obstructing the presenting part. A vaginal septum may also impede progress and may have to be excised. During the third stage of labor the placenta may fail to separate spontaneously and may have to be removed manually. There is also an increased incidence of postpartum hemorrhage.

These complications have raised the fetal mortality to between 23 and 43 per cent and the maternal mortality to between 2 and 2.5 per cent. The fetal and maternal risks are greatest in the uterus bicornis unicollis and uterus subseptus and least in didelphys and in uterus unicornis.<sup>5</sup>

Pregnancy in a rudimentary horn of a uterus bicornis has particular relevance to this report. Eastman<sup>3</sup> stated that by the year 1900 84 cases had

Presented at a meeting of the Brooklyn Gynecological Society, May 15, 1957.

<sup>\*\*</sup>Present address: Jericho, N. Y.

been collected by Kehrer from Germany, and in 1945 Stander<sup>8</sup> stated that this was the most common abnormality. Since 1911, however, only 13 cases had been reported in the American, British, and Indian literature.<sup>2, 7, 9, 10</sup> Of these 13 patients, one died from a ruptured horn at 4½ months' gestation and in another the pregnant horn ruptured but the patient survived. A pelvic mass was diagnosed incorrectly in 3 patients before operation, an ectopic pregnancy in one and missed abortion in 5. Two of the cases were difficult to evaluate. In no case was a correct preoperative diagnosis made.

The patient was a 33-year-old white woman with one living child following a normal pregnancy and delivery in 1954. Her past history did not reveal any abnormality in the menstrual cycle. Her last period was Sept. 1, 1955. The initial examination, during the eighth week of amenorrhea, revealed a palpable mass, approximately 5 cm. in diameter, in the right adnexal region. The uterus was felt to be enlarged to the size of a 6 weeks' gestation. A diagnosis of intrauterine pregnancy complicated by a right ovarian cyst was made. During the fourth month of gestation she began to have irregular vaginal bleeding which occurred once a month until the seventh month. Fetal movements were said to be present in the fifth month and the fetal heart was heard on one occassion during the fifth month.

Fig. 1.

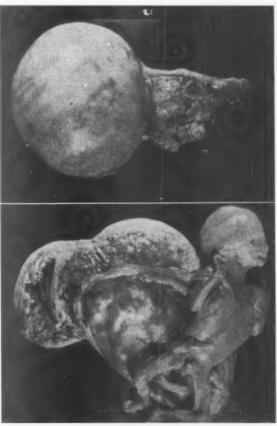


Fig 2.

Fig. 1.—Gross specimen: the rudimentary horn with attached ovary, tube, and corpus luteum.

Fig. 2.—The amniotic sac is opened showing the macerated fetus.

By the sixth month a diagnosis of missed abortion was made on the basis of the absent fetal heart sounds and failure of the uterine size to correspond with the period of gestation. X-ray examination in the sixth and eighth months of amenorrhea revealed a fetus 9 cm. in length with overlapping of the skull bones and marked angulation of the spine.

During the eighth month an attempt to induce labor with intravenous Pitocin was unsuccessful and 2 months later a laparotomy was performed. The uterus was found to be of normal size. The left ovary, tube, and left round ligament were normal. The uterus was displaced to the left by a mass approximately 10 cm. in diameter, on its right side. A fibrous band, 2.25 cm. in length, connected this mass to the mid-portion of the uterus. The right tube, ovary, and right round ligament were attached to the upper right surface of this mass, which proved to be a rudimentary horn. The horn and the attached tube and ovary with its visible corpus luteum were removed (Fig. 1). Subsequent x-ray examination of the horn revealed a fetus within. A careful search for a channel leading to the rudimentary horn was unsuccessful (Fig. 2).

#### Comment

Of the 13 cases reported since 1911, only 2 cases revealed a communication between the rudimentary horn and the uterus. Eastman<sup>3</sup> stated that Kehrer found no communication in 78 per cent of his 84 cases, and from this deduced "that a pregnancy must have followed external migration of the spermatozoa or the fertilized ovum." Of course, failure to find a communicating canal may also result from its apparent obliteration by an enlarging rudimentary horn.

The outcome of a pregnancy in a rudimentary horn will depend upon the presence or absence of a channel between the horn and the uterus. a communication is present the result, as a rule, will be a spontaneous abortion and the diagnosis of a rudimentary horn may be missed. If there is no communication the prognosis is serious for it may lead to a rupture of the horn or a missed abortion.

# Conclusions

- 1. A case of a pregnancy in a noncommunicating rudimentary horn is presented.
- 2. A missed abortion if unusually prolonged suggests a defect in the embryonic development of the genital tract, regardless of the patient's normal obstetrical history.

#### References

- Baker, W. S., Roy, R. L., Bancroft, C., McGaughey, H., and Dickman, H. F.: Am. J. Obst. & Gynec. 66: 580, 1953.
   De Nicola, R. R., and Petersen, M. R.: Am. J. Surg. 73: 381, 1947.
   Eastman, N. J.: Williams Obstetrics, ed. 11, New York, 1956, Appleton-Century-Crofts,
- Inc., p. 641.
  4. Fenton, A. M., and Singh, B. P.: AM. J. OBST. & GYNEC. 63: 745, 1952.
  5. Holmes, J. A.: Brit. M. J. 2: 1144, 1956.
  6. Jarcho, J.: Am. J. Surg. 71: 106, 1946.

- 7. Mulsow, F.: Am. J. Obst. & Gynec. 49: 773, 1945. 8. Stander, H. J.: Williams Obstetrics, ed. 9, New York, 1945, D. Appleton-Century Company, Inc., p. 709.

  9. Stander, R. W.: Obst. & Gynec. 8: 232, 1956.

  10. Waters, A.: Indian M. Gaz. 79: 355, 1944.

# AN UNUSUAL CASE OF RUPTURE OF A PREGNANT RUDIMENTARY HORN OF A BICORNUATE UTERUS\*

JACK A. GOLDMAN, M.D., AND BENJAMIN ECKERLING, M.D. PETACH-TIQVAH, ISRAEL

(From the Department of Obstetrics and Gynecology, The Beilinson Medical Center, Beilinson Hospital)

RELATIVELY few comprehensive studies<sup>1-4</sup> comprising a significant number of cases of congenital malformations of the female reproductive tract associated with pregnancy have appeared in the obstetrical literature.

Among congenital uterine malformations the most frequently encountered is the bicornuate uterus. The report presented is a case of rupture of a pregnant rudimentary horn of a bicornuate uterus.

# Case Report

A. T., an 18-year-old woman, married for 17 months, was admitted to our department in September, 1957. On admission the patient complained of severe pain in the lower abdomen which had started just a few hours previously, nausea, and vomiting. The patient appeared markedly pale and was in shock; the pulse rate was rapid and shallow at 100 to 120 per minute and blood pressure was 80 systolic and 50 diastolic.

Previous history revealed that she had always been well. Menarche had occurred at the age of 13, and periods appeared at regular monthly intervals. The last menstrual period had occurred 4½ months prior to admission. On examination the uterus could be felt at approximately 2 fingerbreadths below the umbilicus. Abdominal palpation revealed marked tenderness and rigidity over the entire abdomen, but particularly over the lower abdominal area. On vaginal examination the cervix was found to be partially effaced and one finger dilated; it contained large fragments of tissue. Moderate bleeding was noticed. The uterus was enlarged to the size of a 3 months' gestation. Next to it and joining it, a soft, globular mass, slightly larger than the uterus, was palpated to the left. The cul-de-sac of Douglas was slightly bulging and tender on examination. It is interesting to note that initially the picture was one of incipient abortion with an additional mass to the left, possibly an ovarian cyst or an ectopic pregnancy.

In order to arrive at a more accurate diagnosis, a further examination was performed with the patient under anesthesia, and a cul-de-sac puncture was made. A considerable amount of blood was obtained; it was therefore decided to proceed with a laparotomy.

When the abdominal cavity was opened, a large amount of old blood and blood clots were found and evacuated. The uterus was the size of a 3 months' gestation, and was soft; on the left side and next to it was another mass, larger than the uterus and connected to it through a pedicle 2 cm. long and 0.5 cm. broad. The vesicouterine fold covered the cervix and lower segment of the uterus as well as the lower pole of the mass. At the upper pole of the mass a large tear was noted, approximately 10 cm. long, and lying in it was the placenta. The umbilical cord led to a well-developed fetus about 22 cm. long, which lay

<sup>\*</sup>Presented at a meeting of the Israeli Obstetrical and Gynecological Society, Tel-Aviv, May, 27, 1958.

freely in the abdominal cavity. From the left side of the mass originated a normal, intact Fallopian tube, ovarian ligament, and the left round ligament. After the vesicouterine fold was dissected off the uterus and the tumor, the latter, including the entire pedicle, was resected together with the left adnexa.

The uterus was opened in the fundal area and a great amount of decidua-like tissue was removed. The uterus was closed and following this the vesicouterine fold was replaced. The abdomen was closed in layers. The postoperative course was uneventful and the patient left the hospital on the thirteenth day after operation in good condition.



Fig. 1.-Gross specimen: ruptured mass with placenta and fetus.

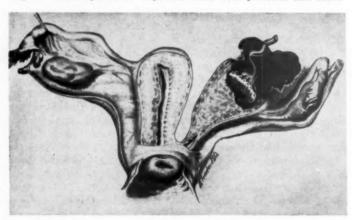


Fig. 2.-View of uterus and ruptured rudimentary horn at operation.

The removed mass (Fig. 1) was found to be a rudimentary horn. Histological examination revealed only atrophic endometrium in the pedicle, no endometrial cavity in a section through the mass, and a small uterine cavity at the upper pole of the rudimentary horn (Fig. 2).

# Comment

Reviewing the literature we found a relatively small number of reported cases of this kind. De Lee<sup>5</sup> stated that Mauriceau and Vassal in 1669 recorded the first case of pregnancy in a rudimentary horn of bicornuate uterus. Kehrer<sup>6</sup> collected 84 cases from the literature until 1899. Reviews by other authors have appeared.<sup>7-12</sup> Mulsow<sup>13</sup> in 1945 reviewed 9 cases, among which 2 had ruptured. Only single case reports<sup>14-17</sup> have been published since then.

In view of the microscopic findings, we may assume that only a small portion of the cervical canal existed in the pedicle, and that there was no communication between it and the small endometrial cavity close to the Fallopian tube. Halban and Seitz<sup>18</sup> have described this possibility in a rudimentary horn.

In view of these facts the question now arises: Where did fertilization take place? Two possibilities exist:

1. Ovulation and fertilization took place on the opposite side, and the fertilized ovum made an external migration to the tube near the rudimentary horn, and implanted in it.

2. Ovulation took place in the overy corresponding to the rudimentary horn, while the spermatozoon effected an external migration, arrived at the opposite side and impregnated the ovum there.

Both possibilities have been described before<sup>19-21</sup> and have been known to occur occasionally. Rupture most probably occurred because of the deformed and distorted uterine musculature commonly found in a bicornuate uterus, and the too narrow space for development of a gestation.

The difficulty in diagnosis prior to operation was due to the size and consistency of the uterus, as well as to the effaced and slightly opened cervix, which simulated the clinical picture of incipient abortion. This misleading picture was explained at operation when an unusually large amount of decidual tissue was removed from the uterus.

Other possibilities, such as interstitial pregnancy and the formation of a true sacculation of the contractile portion of the pregnant uterus, 22 were disproved by clinical findings and by pathological examination.

Consequently, the diagnosis of rupture of a rudimentary uterine horn due to an advanced pregnancy seems to be proved.

# References

- Jarcho, J.: Am. J. Surg. 71: 106, 1946.
   Fenton, A. N., and Singh, B. P.: Am. J. Obst. & Gynec. 63: 744, 1952.
   Baker, Wm. S., et al.: Am. J. Obst. & Gynec. 66: 580, 1953.
   Jones, W. S.: Bull. Margaret Hague Maternity Hosp. 7: 85, 1954.
   De Lee, J. B. and Greenhill, J. P.: Principles and Practice of Obstetrics, ed. 8, Philadelphia, 1943, W. B. Saunders Company, p. 664.
   Kehrer, E.: Das Nebenhorn des doppelten Uterus, Inaugural discussion, Heidelberg, 1899.
   Kussmaul, A.: Wuerzburg, 1859. Cited by Halban and Seitz. 18
   Saenger: Zentralbl. f. Gynäk. 7: 324, 1883.
   Engström, O.: Mitth. a. d. gynaek. Klin. d. O. Engström in Helsingfors 3: 99, 1901.
   Werth: Arch. f. Gynaek. 66: 48, 1905.

d d

- Werth: Arch. f. Gynaek. 66: 48, 1905.
   Beckmann, W.: Ztschr. f. Geburtsh. u. Gynäk. 68: 600, 1911.

- Justi, K.: Ztschr. f. ang. Anat. 3: 163, 1918.
   Mulsow, F. W.: Am. J. Obst. & Gynec. 49: 773, 1945.
   Rademaker, L. A., and Royer, E. L.: Am. J. Obst. & Gynec. 62: 694, 1951.

- 15. Saleh, J. S.: AM. J. OBST. & GYNEC. 70: 426, 1955.
  16. O'Sullivan, D.: J. Obst. & Gynaec. Brit. Emp. 45: 428, 1958.
  17. Speert, H., Nash, W., and Kaplan, I. L.: Obst. & Gynec. 7: 332, 1956.
  18. Halban, J., and Seitz, L.: Biologic und Pathologic des Weibes, Berlin, 1928, Urban & Salvaryaroborg, Bend VII. 7:112.8 Halban, J., and Seitz, L.: Biologie und Pathologie des Weibes, Berlin, 1928, Urban & Schwarzenberg, Band VII, Teil 2, S. 800.
   Beck, A. C.: Obstetrical Practice, ed. 3, Baltimore, 1942, The Williams & Wilkins Com-
- pany, p. 640. 20. Titus, Paul: The Management of Obstetrical Difficulties, ed. 3, St. Louis, 1945, The
- C. V. Mosby Company, p. 141. 21. Eastman, N. J.: Williams Obstetrics, ed. 11, New York, 1956, Appleton-Century-Crofts,
- Inc., p. 641. 22. Rubovitz, Wm. H.: Am. J. Obst. & Gynec. 62: 1044, 1954.

### A ROBERT PELVIS

# Case Report and Review of the Literature

IRWIN H. KAISER, M.D., MINNEAPOLIS, MINN.

(From the Department of Obstetrics and Gynecology, University of Minnesota Medical School)

HEINRICH Ludwig Ferdinand Robert was born in Marburg in 1814, the son of the vice-chancellor of the university. He was educated in Göttingen, Berlin, and Würzburg. In the last city he apprenticed himself to Joseph d'Outrepont whose daughter he later married. He presented his doctoral dissertation in the city of his birth in 1837 and returned there in 1840. Three years later Robert was appointed university lecturer, but in 1850 he resigned to move to Coblenz. In 1863 he at last settled in Wiesbaden where he practiced medicine until his death in 1878.

Robert published 6 monographs during his career. The first 2, his inaugural dissertation and his qualifying paper for the Marburg lectureship, were concerned with the peritoneum and omentum. The final 2 papers, in 1855, dealt with the knee joint. The intermediate pair, the first of which was published in 1842<sup>2</sup> and the second of which appeared in 1853,<sup>3</sup> provide the first description of the severely and symmetrically transversely contracted pelvis which has since borne the author's name.

The Robert pelvis is among the rarest of all types of contracted pelves. Indeed, none has been recorded in the Western Hemisphere.<sup>4</sup> For this reason, the following case is reported.

Mrs. A. was referred to University Hospitals for delivery because her doctor\* had found a contracted pelvis. The narrowness of her hips could be seen by ordinary inspection (Fig. 1). The distance between the iliac spines was found to be 16 cm., between the iliac crests 21 cm., and between the trochanters 26 cm. The intertuberous diameter was less than 7 cm. and the pubic arch was quite narrow. The diagonal conjugate exceeded 11.5 cm.

X-ray films of the pelvis were obtained (Figs. 2 and 3). In the lateral projection, taken with a bar (with markings at centimeter intervals) placed between the buttocks, the only deviations from normal are minimal alterations in the smooth curve of the anterior surface of the sacrum. These projections, which occurred on either side of the intervertebral spaces, were in all likelihood due to rachitic epiphysitis during the third to fifth year of life. The minimal anteroposterior diameter of the inlet was 10 cm.

In the anterior-posterior projection, films for which were taken by the precision parallax technique, it can be seen that the ilia are directed much less obliquely than normally, i.e., they tend toward being parallel to the anteroposterior plane of the patient. In addition, they are deficient in size. The normal width of the sacral alae is also lacking bilaterally, and there is no suggestion of a sacroiliac joint on either side. The result of

<sup>\*</sup>Dr. Mitchell J. Jurdy of Minneapolis, Minn.

these changes is marked transverse narrowing of the pelvis. The iliac spines are prominent and impinge even further on the birth canal. The maximum transverse diameter of the inlet is 8.4 cm. and the distance between the ischial spines is 5.9 cm.

The patient has been delivered twice by elective cesarean section. Her mother has been delivered of a number of children normally. Two of the patient's sisters have also been delivered of term infants vaginally, and a third, still nulligravid, is of normal female build. Her daughter appears to have a normal pelvis at the age of 18 months.

There is no history of illness or injury in the patient's childhood which might be associated with the shape of her pelvis.



Fig. 1.—The narrowness of the patient's pelvis can readily be seen in this photograph taken post partum.

#### Comment

Little<sup>5</sup> has recently discussed the anatomy and etiology of the Robert pelvis and described a contemporary case and two preserved older pelves from Great Britain. He has suggested that the entity be subdivided into 3 categories, the true Robert pelvis, in complete and incomplete forms, and the pseudo-Robert pelvis. In instances of the true Robert pelvis, the transverse diameter of the inlet is contracted in proportion to the diameters of the midplane and outlet, and there is no history of infection or trauma. The further subdivision into complete and incomplete forms is based on the presence or

absence of sacroiliac joints. In the instance of the pseudo-Robert pelvis the inlet is relatively large in its transverse measurements compared with the midpelvis, and there is a history of severe injury or infection of the bones of the true pelvis. Such a classification as this seems entirely proper. Robert's first patient<sup>2</sup> would be an example of complete true Robert pelvis, and his second<sup>3</sup> an example of pseudo-Robert pelvis.

The earliest cases of this entity came to attention at autopsy since a high proportion of the mothers died in obstructed labor. In 1910, in the classical monograph on the subject, Breus and Kolisko<sup>6</sup> gathered together all such cases with postmortem findings. Of the 10 cases so compiled 5 (Robert, Kirchhoffer, Roberts, Kehrer, and Ferruta) belong in the true category and one (Choisil and M. Tremont) cannot be classified because of insufficient data.

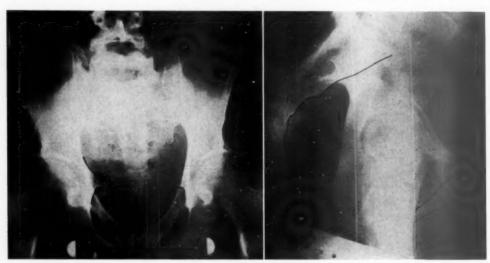


Fig. 2.

Fig. 3

Fig. 2.—Anteroposterior roentgenogram of the patient's pelvis taken post partum. Fig. 3.—Lateral roentgenogram of the pelvis taken post partum.

With the recognition of the clinical entity, it was realized that delivery had to be accomplished by cesarean section, but it was not until 1882 that Ehrendorfer<sup>7</sup> reported the first instance of clinically diagnosed Robert pelvis so treated. Both the mother and infant survived.

In 1913 Beckers recorded the first instance of Robert pelvis in which the diagnosis was made clinically and then confirmed by roentgen examination of the pelvis in a living patient. He and, later, Budniok, who reported a second such case in 1914, reviewed the literature up to that time, particularly in reference to cases described clinically but unconfirmed by autopsy or x-ray.

In 1917, Lazard<sup>10</sup> reported a case from California, unfortunately without either clinical or x-ray measurements, of transversely contracted pelvis following severe trauma to the pelvis in childhood. The patient subsequently was never able to walk erect. If this was a Robert pelvis, it falls into the pseudo eategory.

There are, then, including the cases referred to above and the 3 reported in Little's paper, 10 instances of true Robert pelvis proved by autopsy or x-ray, in the literature to date. The examples of pseudo-Robert pelvis are fewer, being at most 6, but there are a host of reports without either x-ray or autopsy demonstration of the anatomy.

Despite the fact that, in the 116 years since Robert's original description, less than a dozen true instances of the deformity have been reported, the recent record of a contemporary case by Little and the present report indicate that the entity has not disappeared. It is probably neither inflammatory nor dietary in etiology; it is almost certainly a congenital anomaly. Perhaps now that the safety of cesarean section has made it possible for mother and children to survive, a careful study of the children of women with Robert pelvis will clarify possible hereditary aspects of the anomaly. In this regard, reporting of other instances of Robert pelvis, which surely must have been observed, would assist in determining its racial and geographic incidence.

### References

- 1. Hirsch, A.: Biographisches Lexicon der hervorragenden ärtze aller Zeiten und Völker, Berlin, 1932, Urban and Schwarzenberg, Vol. 4, p. 835.
- 2. Robert, F.: Beschrei u. Freiburg, 1842. Beschreibung eines im höchsten Grade querverengtes Becken, Karlsruhe
- 3. Robert, F.: Ein durch mechanische Verletzung und ihre Folgen querverengtes Becken, Berlin, 1853.
- 4. The following reference works were consulted under the headings: Robert; Roberts; Pelvis, deformities of and abnormalities of.
  - a. Index Catalogue of the Surgeon General's Library: 1st, 2nd, and 3rd series.
  - b. Quarterly Cumulative Index Medicus, vols. 3-38, 1928-55.

  - c. Current List of Medical Literature, vols. 29-33, 34, Nos. 1 and 2, 1956-58.
    d. Excerpta Medica, Section X, Obstetrics and Gynecology, vols. 1-10, 11, Nos. 1-10, 1948-
- Little, E. W.: J. Obst. & Gynaec. Brit. Emp. 65: 465, 1958.
   Breus, C., and Kolisko, A.: Die pathologischen Beckenformen, Leipzig u. Wein, 1910, Deuticke, p. 225.
- 7. Ehrendorfer, E.: Arch. f. Gynäk. 20: 101, 1882.
- 8. Becker, K.: Monatsschr. f. Geburtsh. u. Gynäk. 38: 517, 1913.
- 9. Budnick, P.: Ein Fall von Robertschem Becken, Halle a.S., 1914.
- 10. Lazard, E. M.: Am. J. Obst. 76: 585, 1917.

# EVALUATION OF PARAVERTEBRAL LUMBAR SYMPATHETIC BLOCK IN LABOR\*

Lucy A. LaSalvia, M.D., Paul S. Copit, M.D., and V. E. Kondon, M.D., Philadelphia, Pa.

(From the Division of Women, Habnemann Medical College and Hospital)

THE continual search for new analgesic agents to effect a pain-free labor is in itself an indication that our present-day methods leave much to be desired. That pain relief during labor is desirable is generally accepted. The hazards which accompany the administration of various analgesic agents, however, make their limited use both problematic and controversial.

The most popular analysics employed in this country are generally combinations of a sedative (Demerol, barbiturates, morphine, etc.) and scopolamine to produce amnesia. The toxicological and pharmacological effects of these drugs on both mother and infant are well known.

The use of conduction anesthesia methods such as caudal and spinal during labor needs no elaborate discussion. Numerous studies have shown such drawbacks as diminished uterine contractions, respiratory paralysis, increased incidence of forceps deliveries, and technical difficulty of administration, requiring special skill.

Recently, paravertebral lumbar sympathetic block has reportedly been used very successfully for pain relief during labor. This method of conduction anesthesia was first used in 1930 by Aburel, and sporadically since then by Cleland, de Bellefkoid, Shumacker and associates, Jarvis, Snoeck and Pirson, and others. In 1953, Reich reported enthusiastically on results obtained in 800 patients in labor, with the use of this method.

In recent years the afferent pathways to the uterus, conducted through the sympathetics, have become better understood and localized at the level of the eleventh and twelfth thoracic roots. It seems logical, therefore, in labor to employ a regional anesthetic to block these sensory nerves without appreciably affecting the motor nerves of the uterus.

The object of the present study is to evaluate the use of bilateral paravertebral lumbar sympathetic block as an anesthetic method in labor; its uses, advantages, disadvantages, and practicability for general use.

#### Method

The method employed here was essentially the same as described by Reich<sup>1</sup> in 1951. Each patient received a barbiturate ( $1\frac{1}{2}$  grains of Seconal or Nembutal) about half an hour prior to the injection, to counteract possible sensitivity to Intracaine.

Presented at a meeting of the Philadelphia Obstetrical Society, February, 1957.

We employed a 1 per cent Intracaine solution, using 25 c.c. on each side, and injecting slowly at first to note unfavorable "caine" reactions.

The anesthetic agent was injected "bilaterally in the area at which the lumbar sympathetic chain descends at the region of the first lumbar vertebral body, located well anteriorly along its lateral anterior surface." Two 4½ inch needles of special gauge, which permit the threading of polyethylene catheters through them were used. The needles were removed and the catheters left in place, allowing for subsequent reinjections of the anesthetic agent if necessary.

The patient's blood pressure, pulse rate, the fetal heart rate, plus the degree of cervical dilatation, effacement, and station of the presenting part were first recorded.

These findings were again recorded 5 minutes after injection. The blood pressure, pulse rate, and fetal heart rate were then followed at 15 minute intervals for the first hour and at 30 minute intervals thereafter.

# Technique

Paravertebral lumbar sympathetic block is administered when it has been definitely established that the patient is in active labor and requires sedation (usually at 3 to 5 cm. dilatation). Injection is accomplished in the labor room, with the patient sitting with her legs over the side of the bed, arching her back forward.

The skin of the back is prepared with a suitable antiseptic and draped with towels. With the iliac crests as the landmark corresponding to the fourth lumbar vertebra, the second lumbar vertebra is located. Skin wheals are made on the left and right sides, 2 inches from the upper border of the second lumbar vertebra on each side. A special 6 inch, 18 gauge needle, with a stylet, is introduced through the skin wheal at a 15 or 20 degree angle, toward the median line (Fig. 1). As the tip touches the vertebral body, it is withdrawn slightly and directed anteriorly off the vertebra for another centimeter. In the average patient the needle will then be approximately 33/4 to 4 inches from the skin. A similar needle is placed through the skin wheal on the other side. Before injection of the anesthetic agent, careful aspiration with a dry syringe is done, in four quadrants, to ascertain that neither blood nor spinal fluid is obtained. Then 25 c.c. of 1 per cent Intracaine solution is injected slowly, first on one side, then the other.

After injection, polyethylene catheters are threaded through each needle for use in subsequent injections if necessary, and the needles are removed. The ends of the catheters are sealed with sterile stoppers and covered with sterile dressings (Figs. 2 and 3).

Reinjections of 25 c.c. of 1 per cent Intracaine are used as required for continued pain relief until the perineal stage. At this time the patient requires additional anesthesia for delivery, since lumbar sympathetic block cannot affect the somatic nerves of the perineum (pudendal and ilioinguinal).

#### Results

The 200 patients used in this study were all ward patients with the exception of an insignificant few (Table I).

The indications for cesarean section were (1) cephalopelvic disproportion, (2) uterine inertia, and (3) failed Pitocin induction following a period of prolonged ruptured membranes.

We did not note any appreciable change in the tone or duration of uterine contractions following the block, other than a transitory diminution of contractions immediately following injection in some cases.



Fig. 2.



Fig. 3.

Fig. 1.—Angle of needles.
Fig. 2.—Needles in place. Catheters in needles.
Fig. 3.—Catheters in place. Needle stops inserted.

TABLE I. PARITY AND TYPE OF DELIVERY

		NO.	
Parity.—			
Nullip	arous	134	
Multip		66	
Type of $\dot{D}$			
Sponts		90	
	forceps	40	
	orceps	53	
Midfo		12	
	ean section	3	
	(assisted)	1	
	(extraction)	1	

TABLE II. CHANGES IN BLOOD PRESSURE AND PULSE RATE FOLLOWING BLOCK

	AVERAGE DROP
Systolic blood pressure	14.8 mm. Hg
Diastolic blood pressure	14.1 mm, Hg
Pulse rate	1.7 beats/min.

A drop in blood pressure usually occurred within the first 15 minutes following the block, but occasionally was noted as long as one hour following injection. While the average drop was about 14 mm. Hg (occurring in 163 patients), 70 of these patients showed a drop of 20 mm. Hg or more. The highest drop was 72 mm. Hg systolic pressure, and 66 mm. Hg diastolic pressure (Table II).

Ephedrine sulfate and/or intravenous glucose were used to combat drops in blood pressure and were usually effective within 15 to 20 minutes.

The pulse rate was at times variable, but remained stationary in the majority of cases. It dropped as low as 24 beats in one instance, and rose as high as 40 beats in another. There was no correlation between change in blood pressure and change in pulse rate.

It is apparent that there was some change in cervical dilatation following the paravertebral sympathetic block in the majority of cases (Tables III, IV, and V). In 36 cases, cervical dilatation progressed rapidly and was shown to be more than 3 cm. greater than on initial examination. This emphasizes the need for close observation lest the patient be delivered in bed.

TABLE III. CHANGE IN CERVICAL DILATATION AFTER BLOCK

	NO. CASES	%
No change	81	40.5
Increased	119	59.5
1 cm. change	48	24.0
2 cm. change	71	35.5

TABLE IV. CHANGE IN CERVICAL EFFACEMENT AFTER BLOCK

	NO. CASES	%
No change	155	77.5
Progressive	45	22.5
	Average in above 45 cases	19.8

Pain relief following injection was almost always immediate and dramatically complete (Table VI). The initial injection produced anesthesia for periods of time varying from one hour up to 5 hours. Reinjection through the polyethylene tubing did not seem to produce anesthesia for an equivalent period of time compared with the first injection. Reinjections were given at 1½ to 3 hour intervals as required by the patient, up until the perineal stage, when supplemental anesthesia was given.

TABLE V. CHANGE IN STATION AFTER BLOCK

	NO. CASES	%
No change	124	62
Change of 1 cm. or more	76	38

TABLE VI. PAIN RELIEF AND DURATION OF LABOR FOLLOWING BLOCK

	DILATATION		LENGTH OF LABOR	
	Gravida i			
	Less than 5 cm.	,	6 hours 2 minutes	
	More than 5 cm.		3 hours 58 minutes	
	Gravida ii.—			
	Less than 5 cm.		2 hours 4 minutes	
	More than 5 cm.		1 hour 8 minutes	
	Gravida iii.—			
	Less than 5 cm.		2 hours 52 minutes	
	More than 5 cm.		1 hour 56 minutes	
Avera	ge period of pain relief after block			
	(each injection)		2 hours 30 minutes	

TABLE VII. TYPE OF ANESTHESIA FOR DELIVERY

ANESTHETIC	NO. OF CASES
Pudendal block	94
Saddle block	46
None	27
Gas, oxygen, ether	12
Local	11
Nitrous oxide and oxygen	8
Ether	2

No supplemental anesthesia was given in cases in which labor was so rapid that time did not permit additional anesthesia or in those in which additional relief of pain was not required.

A bloody tap was not a contraindication to injection (Table VIII). The needle was merely withdrawn and reinserted 0.5 cm. lateral and cephalad to the original site. If no blood was then aspirated we proceeded with the injection of Intracaine.

When spinal fluid was aspirated, again the needle was removed and reinserted at a different angle.

In order to avoid painful injections a small amount of Intracaine was deposited in the tissues as the needles were inserted.

TABLE VIII. COMPLICATIONS

COMPLICATION	NO. OF CASES
 Bloody tap	43
Spinal fluid tap	1
Painful injection	75
Plastic tubing retained in back	1
Postpartum hemorrhage	0

The patient with a piece of plastic tubing in the tissues of her back was seen by a neurosurgeon, who advised leaving the tubing in place. It was felt that this inert substance would produce little if any difficulty.

TABLE IX. MATERNAL AND FETAL MORTALITY

Maternal deaths	0
Stillbirths	2
Neonatal deaths	1

The 2 stillborn infants were premature, weighing 2 pounds, 2 ounces, and 2 pounds, respectively (Table IX). These fetal deaths were in no way related to the paravertebral block. Also, the one neonatal death which occurred in this series was again that of a premature infant weighing 2 pounds, 4 ounces. This too had no relationship to the type of analgesia used.

# Advantages

- 1. Complete, immediate pain relief.
- 2. Lack of maternal cerebral depression. Patients are awake, alert, cooperative.
  - 3. Lack of fetal respiratory depression.
- 4. Especially useful in premature labor, where sedation is contraindicated.
  - 5. No interference with uterine contractility.
  - 6. Does not produce or contribute to postpartum hemorrhage.
  - 7. Aids cervical dilatation inasmuch as pain relief relieves tension.
- 8. Can be used in patients with chronic lung disease, asthma, or any other systemic disease which contraindicates use of sedatives systemically.
  - 9. Of value in postmaturity where fetal oxygenation is problematic.
  - 10. Spontaneous delivery, low or outlet forceps may be anticipated.

# Disadvantages

- 1. Possibility of injection into a blood vessel.
- 2. Possibility of intrathecal injection.
- 3. Some pain with injections in a significant number of patients.
- 4. Danger of breakage of polyethylene tubing in tissue of back.
- 5. Technical skill is required. Despite the fact that this procedure seems relatively simple, we should not underestimate the skill required to accomplish any type of nerve block.
- 6. A physician must be in constant attendance throughout labor. This fact alone makes this method impractical for use by general practitioners or obstetricians who do not practice in a group.
- 7. Cephalopelvic disproportion and uterine inertia may be overlooked and not diagnosed early enough since the patient experiences no pain of uterine contractions. This necessitates following labor by constant manual palpation of uterine contractions.
- 8. Contraindicated with prenatal hypotension, history of back injury or chronic backache, skin infection of the back, severe toxemia (labile vasomotor system).

# Summary and Conclusions

Two hundred cases of paravertebral lumbar sympathetic block for analgesia in labor are presented. The indications, contraindications, advantages, and disadvantages are presented.

It appears that this type of conduction anesthesia, in the hands of trained obstetricians, is a valuable adjunct to our armamentarium of obstetrical analgesia.

We wish to thank Dr. Newlin F. Paxson and the entire resident staff for their cooperation. We also wish to express gratitude to Dr. William G. McCain for his clinical assistance and excellent photography.

# References

- Reich, Arthur M.: Am. J. Obst. & Gynec. 61: 1263, 1951.
   Reich, Arthur M.: Obst. & Gynec. 1: 672, 1953.
   Jarvis, Shiras M.: Am. J. Obst. & Gynec. 47: 335, 1944.
   Cleland, J. G. P.: Surg. Gynec. & Obst. 57: 51, 1933.
   Lull, C. B., and Hingson, R. A.: Control of Pain in Childbirth, ed. 3, Philadelphia, 1948, J. B. Lippincott Company.
   Shumacker, H. B., Manahan, C. P., and Hellman, L. M.: Am. J. Obst. & Gynec. 45: 129, 1943.
   Penman, W. Robert: S. Clin. North America 34: 1551, 1954.
   de Bellefkoid, G.: Rev. franç. de gynéc. et d'obst. 34: 251, 1939.
   Snoeck, J., and Pirson, C.: Acta clin. belg. 2: 157, 1947.

1930 CHESTNUT STREET

# GANGRENE AFTER USE OF GAMMA-DIMETHYLAMINO-N-PROPYL PHENOTHIAZINE HYDROCHLORIDE (PROMAZINE)

A Case Report

James H. Shell, Jr., M.D., Davis B. McIntyre, Jr., M.D., and James Castellano, M.D., Baltimore, Md.

(From Saint Agnes Hospital)

FOR some time promazine has been used for obstetrical analgesia with good results. Usually it is used in conjunction with barbiturates, scopolamine, and Demerol. This paper is to report such a use, and to discuss the gangrene that resulted. One author has reported two similar complications with promazine.

A 30-year-old woman, para 2-0-0-2, was admitted in early labor to Saint Agnes Hospital. Past history revealed that this patient had had pyelitis during her first pregnancy and later had developed renal calculi. Thrombophlebitis developed in the second pregnancy requiring saphenous ligation. She had had bronchopneumonia 5 times. She is an average smoker, but during the month prior to delivery, she had smoked excessively because of nervous tension.

At 3 cm. dilation, 200 mg. of pentobarbital sodium, and 0.4 mg. scopolamine were given intravenously without difficulty in the right antecubital vein. At 5 cm. dilation, 50 mg. promazine and 50 mg. Demerol were begun intravenously in the same vein. The patient complained of pain as soon as the injection was begun, and it was discontinued. It was given then in the left antecubital vein. Less than 0.5 c.c. had been given intravenously in the right antecubital vein.

Labor and delivery were uneventful. Approximately 6 hours after the injection, the patient's right arm, distal to the elbow, became cold and slightly cyanotic. This condition responded to heat. The next morning, however, pain, edema and cyanosis of the hand developed. Brachial, radial, and ulnar pulses were all good. Repository heparin was begun, and oral anticoagulants were started after routine associated blood studies were made. Tolazoline hydrochloride (Priscoline), 25 mg. every 4 hours, was administered. In spite of this the cyanosis progressed. Intravenous procaine was begun and papaverine was then given intramuscularly. Although the edema subsided, the process did not abate. On the fifth postdelivery day, the small finger was gangrenous and all digits were cyanotic, the thumb and middle fingers being worse. Three weeks post partum a wet gangrenous process was evident. At 6 weeks post partum it was necessary to amputate the distal phalanx of each finger and of the thumb. Postoperatively the patient did well.

### Comment

In view of the seriousness of this case, it was felt that it should be presented. It is of interest that this and the 2 previously reported cases¹ all showed pain on initial intravenous injection. Although other drugs were used, it is the

belief of the authors that promazine was probably the offender. Opensky¹ stated that the arterial spasm and thrombosis might well be due to infiltration of the promazine into the soft tissues or reflexly through vein irritation after the intravenous injection. Farrar² stated that perivascular infiltration, inadvertent arterial penetration, or injection into a previously damaged vein may produce thrombophlebitis or reflex arteriolar spasm in susceptible subjects. We believe promazine should not be used intravenously.

#### References

- 1. Opensky, M.: J. A. M. A. 168: 1224, 1958.
- 2. Farrar, G. E., Jr.: Wyeth Letter to Physicians, February, 1959, p. 2.

# SPONTANEOUS DETACHMENT OF THE CERVIX DURING LABOR

d

le

y

JOHN GARRY, M.D., BEVERLY, MASS.

(From the Department of Obstetrics and Gynecology, Beverly Hospital)

SPONTANEOUS necrosis with resultant detachment, avulsion, or amputation of the cervix uteri is a rare complication of labor. Ingraham and Taylor¹ have reviewed the world literature on this subject and discovered 54 reported cases up to 1947. Since their comprehensive article occasional reports of one or 2 additional cases may be found in the literature. Finn² in 1950 reported on 5 cases of cervical detachment in 56,000 deliveries at the New York Hospital. The vast majority of reported cases represent partial annular detachment, the detachment having been completed at the time of delivery by the attending physician. The case reported here represents one of total spontaneous detachment.

# Case Report

M. C. was a 31-year-old gravida iii, para ii, Japanese war bride. Her 2 previous pregnancies had been uneventful and had been terminated, following normal average length labors, by simple vaginal delivery. Her largest newborn had weighed 8 pounds, 7 ounces. The patient's prenatal course was uncomplicated; weight gain totaled 24 pounds; blood pressure, urinalysis, and hematological examinations were repeatedly within normal limits. She entered the hospital 5 days after the estimated date of confinement. The bag of waters was intact and the vertex was presenting in the left occipitoposterior position at the pelvic inlet. Rectal examination revealed the cervix to be 2 cm. dilated, approximately 50 per cent effaced, and somewhat firm.

Five hours after admission the amniotic sac ruptured spontaneously. Labor had improved; contractions were strong and regular at 5 minute intervals.

Nine hours after admission cervical dilatation could not be determined, the presenting part was high, and x-ray pelvimetry was performed. X-ray revealed a term infant, with the vertex presenting in the left occipitoanterior position. The true conjugate was 12 cm.; the transverse inlet, 11.5 cm.; and the bispinous diameter, 10.5 cm. Uterine contractions had become more forceful and frequent, a moderate to profuse bloody show was noted, and the patient began to "bear down" with each contraction.

Twelve hours after admission labor continued to be excellent but the cervical dilatation could not be made out rectally. Sterile pelvic examination revealed the vertex at the spines and a thick spongy tissue mass (presumed to be the edematous posterior lip of cervix) was palpable posteriorly.

Fourteen hours after admission the head was in sight and the patient was taken to the delivery room, anesthetized, prepared, and draped for delivery. Pelvic examination revealed the vertex to be anterior and on the perineum. The thick spongy mass previously felt was found lying free in the vagina and was removed. A tentative diagnosis of detachment of the cervix was made. A normal 7 pound, 13 ounce, female infant was delivered with low forceps and without difficulty. The placenta was manually removed. The interior of the

uterus was manually explored and found to be intact; however, no remaining cervical tissue could be palpated. There was no excessive bleeding. Both mother and infant left the delivery room in apparently good condition and were discharged home on the fifth postpartum day.

Pathological Report.—Pathological examination revealed a flat, irregular, hemorrhagie, and edematous reddish-purple mass of tissue which measured 13.2 by 6.5 by 2.4 cm. Microscopic examination showed markedly edematous hemorrhagic connective tissue with a stratified squamous epithelial lining. Blood vessels were markedly dilated and the stroma showed edema with extensive necrosis. Multiple mucous glands were present within the stroma below the epithelium. The final diagnosis was cervical ring with hemorrhagic necrosis.

Pelvic examination of the patient 6 weeks post partum was essentially normal except for almost total absence of palpable or visible cervical tissue. A small puckering of tissue with the centrally located os was present in the vaginal apex, giving the appearance of a post-operative high amputation of the cervix.

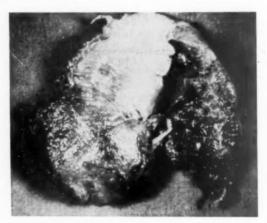


Fig. 1.—Gross specimen showing entire ring of the cervix.

#### Comment

It is an exceptionally traumatic experience to examine a patient at the time of delivery and to withdraw a hand full of cervix! One immediately conjures up in his mind's eye the picture of exsanguinating postpartum hemorrhage, the need for emergency hysterectomy, or the possibility of multiple fistulas or at least a single persistent one. Fortunately most reported cases tend to prove these do not occur. Of the 54 cases reviewed by Ingraham and Taylor, none had bleeding from the site of cervical detachment. Fistula formation was an infrequent complication and emergency hysterectomy was rarely if ever indicated.

The long delay prior to our performing a vaginal examination in this case is regrettable. Apparently the cervix dilated up to about 5 cm. and after that gradually became more and more edematous and hemorrhagic until ultimately it became necrotic and was detached at the pressure site. By the time sterile vaginal examination was performed, the cervix had become partially, if not totally, detached, but because of its position this was not recognized and it was passed off as merely an edematous posterior lip. The pelvis was obviously adequate. Descent of the presenting part was undoubtedly delayed until the unyielding cervix had been removed by necrosis. The failure of the patient to experience postpartum hemorrhage from the site of detachment is simply explained by thrombosis of the vessels secondary to the prolonged pressure.

A certain divergence of opinion regarding handling of future pregnancies is noted in the literature. The majority of authors1, 2, 4 agree that elective section is indicated, although there are those<sup>5</sup> who feel that one should anticipate subsequent delivery from below and interfere only for other reasons. It is doubted that the patient under discussion could successfully carry another pregnancy to the point of viability unless some type of anatomic repair

such as that suggested by Lash<sup>6</sup> were undertaken. The cause of detachment of the cervix has been sought in many areas.2, 3, 7, 8 Detachment is caused by pressure of the presenting part with resulting edema and necrosis of the cervix. No histological abnormalities are found in these detached cervices. Prolonged labor, posterior presentations, contracted pelves, and early rupture of the membranes have been singled out as contributing factors. 1, 2 Certainly it would appear that a long labor with resultant longstanding pressure on the cervix would be necessary to result in necrosis. However, I believe the long labor is not due to the above-mentioned factors but is directly caused by the unyielding cervix. It is logical to consider cervical detachment as the end result of true cervical dystocia. There is much evidence9 to support the thesis that the cervix must be conditioned for labor. The differences between the "ripe" and "unripe" cervix have been cataloged in many articles. Presently there is some opinion that relaxin¹0 may be the hormone responsible for this conditioning. It seems reasonable to assume that the firm "woody" or "unripened" cervix and the cervix that necroses during labor represent varying degrees of the cervix poorly conditioned for labor. That a cervix is allowed to become so edematous as to necrose and slough off is solely the responsibility of the attending physician and represents either failure to pay close enough attention to the condition of the cervix or an error in judgment. Obstetricians experience a natural reluctance to perform a cesarean section in

edematous cervix. Possibly further investigation into the role and clinical efficacy of relaxin in cervical dystocia will prove beneficial in these cases. If nothing else is learned from reviewing the subject of spontaneous detachment of the cervix, it should be apparent that cesarean section is occasionally indicated for cervical dystocia.

the presence of an adequate pelvis. This is carried to the ultimate degree in the patient who is allowed to continue labor in the presence of an undilating

### Summary

A case of total spontaneous detachment of the cervix during labor is

A brief discussion of some of the possible contributing and etiological factors is presented.

#### References

- 1. Ingraham, C. B., and Taylor, E. S.: Am. J. Obst. & Gynec. 53: 873, 1947.
- Finn, W. F.: AM. J. OBST. & GYNEC. 59: 667, 1950.
- 3. Tisdel, J. H., and Andreson, P. S.: Am. J. OBST. & GYNEC. 70: 193, 1955.
- Dippel, A. L.: Postgrad. Med. 16: 282, 1954.
   Epstein, J. R.: Am. J. OBST. & GYNEC. 41: 899, 1941.
- 6. Lash, A. F., and Lash, S. R.: Am. J. Obst. & Gynec. 59: 68, 1950.
- Reekie, R. D.: West. J. Surg. 49: 581, 1941.
   Westerman, M. D.: Brit. M. J. 2: 606, 1942.
- 9. Stone, M. L., Sedlis, A., and Zuckerman, M.: Am. J. Obst. & Gynec. 76, 544, 1958.
  10. Reid, D. E.: In discussion of Stone and associates.

# INVERSION OF THE PUERPERAL UTERUS MANAGED BY THE HAULTAIN TECHNIQUE\*

A Case Report

CHARLES L. EASTERDAY, M.D., AND DUNCAN E. REID, M.D., BOSTON, MASS.

(From the Boston Lying-in Hospital and the Department of Obstetrics, Harvard Medical School)

INVERSION of the puerperal uterus with its attending mortality remains a formidable problem. The purpose of this report is to present a case of uterine inversion treated by the method of Haultain and briefly to consider the more controversial aspects of the management of this complication. The procedure of Haultain has rarely been mentioned in the American literature,<sup>2</sup> although it seems an ideal method of treatment in those cases of inversion approached abdominally and not easily reduced by the method of Huntington.<sup>3, 4</sup>

A 21-year-old primigravida at term was admitted in early labor to a small community hospital. After approximately 8 hours of labor, the membranes ruptured spontaneously and after one hour of second stage labor, with the caput visible, the patient was delivered by low forceps, following which 5 units of Pituitrin was administered. Fifteen minutes after completion of the second stage of labor, the placenta was removed manually with considerable difficulty and was accompanied by profuse bleeding. A unit of blood was given, and 4 hours later the patient was returned to her room. The hemoglobin determination taken at this time was reported as 10.8 Gm.

During the next 4 days the patient continued to ooze slowly per vaginam. The hemoglobin level fell to 6.1 Gm., and the patient was given 500 e.c. of blood. She was moderately febrile with a temperature of  $100^{\circ}-102^{\circ}$  F., but the pulse remained within the range of 100 beats per minute.

Because of continuous vaginal bleeding, the patient was re-examined and by direct inspection the diagnosis of inversion of the uterus was made. It was thought at the time that placental tissue was present over the surface of the inverted uterus. An attempt to remove this precipitated serious hemorrhage, and the vagina was packed tightly with gauze. The patient then received approximately 1,500 c.c. of blood.

One week following delivery, it was decided, after consultation, to examine the patient in the operating room with preparations made for laparotomy. The patient was anesthetized. Palpation of the lower abdomen failed to outline the uterine corpus. The vaginal pack was next removed and this provoked profuse hemorrhage. The vagina was quickly and gently palpated; this examination revealed a marked edematous inverted uterus which filled the vagina and was estimated to be the size of a large grapefruit. The patient was prepared for laparotomy, and the abdomen was opened in a lower midline incision. Inspection revealed the corpus of the uterus to be completely inverted with a resultant cavity 6 inches in depth. Prolapsed into this cavity were the Fallopian tubes, round ligaments, and ovaries. The cervical ring barely admitted one finger, and it was impossible to reduce the inversion by traction on the round ligaments in accordance with the Huntington technique.

<sup>\*</sup>Read before a meeting of the Obstetrical Society of Boston, Jan. 20, 1958.

The cervical ring was quickly incised posteriorly in the manner of Haultain, permitting easy reduction of the inverted uterus. In the usual case this 5 to 6 cm, incision is closed and the uterus left in situ. The posterior area was selected for the incision to avoid the bladder, the upper part of which had been drawn into the inverted uterine cavity.

Examination of the inner uterine surface through the posterior uterine incision revealed the anterior uterine wall covered by dark brown shaggy material. This firm area did not separate readily from the myometrium, and it was thought to represent a placenta accreta. In view of this finding, it was elected to do a supracervical hysterectomy. The patient's condition precluded the additional time and risk involved in performing a complete hysterectomy. A subsequent cervicectomy was easily performed vaginally a few months later. During the hysterectomy the patient received 500 c.c. of blood followed by 1,000 c.c. thereafter. The patient's general condition was satisfactory, and her convalescence was without event. Thirty-six hours after the operation the patient was afebrile, and she was discharged on the tenth postoperative day.

).,

1)

ne

re

re

gh ed

nd by ter ole urs

ely of

me to

ze.

ent

ed.

vas

tly

the

for

led

th.

he

by

The pathologic examination of the uterus revealed the placental site to measure 10 cm. in diameter. This area was covered by tough, shaggy, purplish-red tissue which could not be separated from the underlying endometrium. A few blunt polypoid lobules of hemorrhagic tissue in this adherent mass were thought to be placental tissue. Microscopic examination, however, showed acute massive thrombophlebitis of the placental site with infarction and no evidence of placental tissue (Fig. 1). The specimen serves to demonstrate the pathologic changes which occur in the inverted portion of the uterus and how these changes militate against successful vaginal reduction of the inversion.

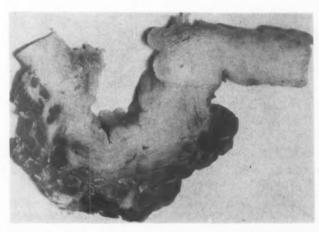


Fig. 1.—Inverted uterine wall with marked thrombosis of decidual vessels of placental site.

#### Comment

Although it is generally conceded that mismanagement of the third stage of labor is an important etiological factor, it is well to recall that at least 40 per cent of the cases of puerperal inversion of the uterus occur where the placental stage has been entirely normal. McCullagh<sup>7</sup> has pointed out that all but 5 per cent of inversions occur within 2 hours after delivery. Consequently, Kaltreider and West<sup>5</sup> have suggested that routine vaginal examination should follow delivery if uterine inversion is to be detected early.

With the constricting effect of the cervical ring, the inverted body of the uterus soon becomes swollen from venous engorgement and edema, and it may, within a few hours, enlarge sufficiently to distend the vagina. Kellogg<sup>6</sup> believed that no one method of management would suffice and that patients should be individualized. He suggested that cases be classified as follows: (1) an acute inversion is discovered before there is cervical ring formation, i.e., in the course

of the third and fourth stage of labor; (2) the diagnosis of subacute inversion is made after cervical ring formation; (3) chronic inversion includes all those neglected cases which already have passed through the subacute stage. Various statistical reviews indicate the validity of this classification as it relates to treatment.1

Immediate manual replacement is invariably successful when the inversion is recognized at the time it occurs. If recognition is delayed, attempts at vaginal replacement may fail, in which case the patient may be lost from hemorrhagic shock. Therefore, by the time the inversion has reached the subacute stage as described by Kellogg, operative reduction seems preferable. In the case reported in detail, it was felt that manual vaginal reduction would be both impossible and disastrous. Persistence in the Huntington technique possibly would have reduced the inversion; however, the Haultain procedure was most expeditious and less traumatic. It is evident that this is an excellent method when the surgeon is faced with a patient who is in poor condition at the time of operation.

Although the placental site was infected and the patient was moderately febrile, in retrospect one must question whether the hysterectomy was a neces-There was the risk of puerperal sepsis, but presumably it could have been controlled by vigorous antibiotic therapy, and, after all, the patient was a young woman with only one child. Some solace was gained by the fact that the mistaken diagnosis of placenta accreta was made on gross examination by a most experienced pathologist. Only on microscopic examination was placenta accreta excluded.

# Conclusion

If recognition of inversion of the uterus is delayed, shock therapy must be instituted, and consideration given to reduction of the inversion by an abdominal approach. The Huntington procedure usually suffices, but when this fails, the Haultain operation facilitates the reduction as exemplified by this case report.

#### References

- Bell, J. E., Jr., Wilson, G. F., and Wilson, L. A.: Am. J. Obst. & Gynec. 66: 767, 1953.
   Haultain, F. W. N.: Proc. Soc. Med. 1: 279, 1908.

- 3. Huntington, J. L.: Boston M. & S. J. 184: 376, 1921.
  4. Huntington, J. L., Irving, F. C., and Kellogg, F. S.: Am. J. Obst. & Gynec. 15: 34, 1928.
  5. Kaltreider, D. F., and West, G. B.: Bull. School Med. Univ. Maryland 31: 145, 1947.

- Kellogg, F. S.: AM, J. OBST. & GYNEC. 18: 815, 1929.
   McCullagh, W.: J. Obst. & Gynaec. Brit Emp. 32: 280, 1925.

# A STUDY OF STAPHYLOCOCCIC COLONIZATION OF POSTPARTUM MOTHERS AND NEWBORN INFANTS\*

Comparison of Central Care and Rooming-In

111

n a-

ie h

V

st

e d

sre a

ie a

ta

st

b-

is

is

28.

THADDEUS L. MONTGOMERY, M.D., ROBERT I. WISE, M.D., WARREN R. LANG, M.D., ROBERT J. MANDLE, PH.D., AND MARYANN FRITZ, M.S., PHILADELPHIA, PA.

(From the Department of Obstetrics and Gynecology, the Department of Medicine and the Department of Bacteriology and Immunology, Jefferson Medical College)

A CURRENT problem of vital importance in hospital practice is the role that antibiotic-resistant staphylococci play in infections of maternity patients and of the newborn.

Staphylococci are ubiquitous microorganisms, gram-positive, catalase-positive, nonmotile, spherical, occurring singly, in pairs, or in irregular clusters. They are facultative anaerobes and are among the easiest of microorganisms to cultivate in vitro. They are classified, according to coagulase production and the ability to ferment mannitol, into two species,  $Staphylococcus\ epidermidis\ (albus)$  and  $Staphylococcus\ aureus$ . S. aureus is coagulase-positive, ferments mannitol, and often produces powerful exotoxins. It is thus the more pathogenic species.<sup>1</sup>

For a number of years it has been observed in hospitals throughout the world that staphylococci cultured from attending personnel and patients have developed resistance to penicillin (probably because of the production of penicillinase by the bacteria) and to broad spectrum antibiotics such as the tetracylines and chloramphenicol as well as to such specific antibiotics as novobiocin and erythromycin. This change, the suppression of drug-sensitive staphylococci and their replacement by drug-resistant ones, seems to be the result of the excessive use of antibiotics in the hospital. In some hospitals penicillin-resistant staphylococci comprise 80 per cent of all those cultured.<sup>2</sup> To date this change has fortunately apparently not occurred to any great extent outside institutions and hospitals. It is difficult to say whether mutation to antibiotic-fastness with staphylococci develops in vivo or whether resistant strains are selected from a heterogeneous population after competing antibiotic-susceptible strains are eradicated. The latter explanation appears more likely.<sup>3</sup>

The purpose of this particular study is to determine the occurrence of hospital-acquired, antibiotic-resistant staphylococci in mothers and newborn

<sup>\*</sup>Presented at a meeting of the Obstetrical Society of Philadelphia on April 3, 1958.

infants cared for on our obstetric and nursery services. Special attention has been given to determining the effect of a modified rooming-in plan with early discharge on the ward service versus central nursery care and relatively late discharge from the hospital on the private service.

# Outline of Study

The proposed scope of the investigation is outlined in Table I. Fifty mothers and babies on the private service and fifty mothers and babies on the ward service were to be studied. Briefly, our intent was to culture secretions from the nose and vagina of each mother on admission, the breast milk on the third day, and secretions from the nose at the time of discharge. Cultures were taken from the nose and periumbilical skin of the newborn at the time of discharge. An effort was made to perform nasal cultures on all personnel, both professional and nonprofessional, having contact with the mothers and their babies. This included physicians, nurses, aides, and auxiliary personnel. Various fomites were also cultured. An attempt was made to obtain cultures of any infections that might occur during the course of the study. Mothers and babies were followed in the home by medical students approximately 10 to 12 weeks after discharge. At that time cultures were again taken from the noses of mothers and babies.

TABLE I. OUTLINE OF STUDY

SOURCES OF CULTURES	TIME OF CULTURE	TYPE OF CULTURE
Mothers	On admission	Nasal and vaginal
	Third day	Breast milk
	At discharge	Nasal
Babies	At discharge	Nasal and periumbilical
Husbands	~	Nasal
Personnel		Nasal
Fomites in patient rooms, nurseries, de- livery rooms, formula room		
Specific infections		
Follow-up of mothers and babies in the		
home	10-12 weeks after discharge	

An over-all summary of the total number of cultures taken (1,222) is presented in Table II. These included cultures from 24 staff physicians (17 obstetricians, 7 pediatricians); 7 members of the house staff (5 obstetric residents, 2 pediatric residents); 41 graduate nurses and 26 student nurses. Cultures were obtained from 53 mothers on the private service and from an equal number on the ward service as well as from babies on both services and from 29 fathers on private and 23 on ward service. In addition, cultures were obtained from 17 auxiliary personnel (maids, electricians, hematology technicians, etc.). Moreover, many cultures were taken from the delivery suite, the nurseries, and ward, private rooms, and the formula room.

Technique.—Nasal cultures were obtained by firmly rotating a sterile, moistened, cotton-tipped applicator in both nostrils. A Petri dish containing glycine tellurite media<sup>4</sup> was inoculated promptly; then the applicator was returned to a small test tube containing 1.0 ml. trypticase soy broth. The plates were incubated for 48 hours at 37° C. If no growth was obtained, a second plate was streaked with broth from the test tube. Skin cultures were obtained by swabbing the periumbilical area with a moistened applicator and proceeding as above. Air samples were obtained by the use of a modified slit air

959

las

rly

ate

fty the ons the res me lel, res ers 10

ore-

(17)

esi-Cul-

ual

rom vere hnithe

rile, ing re-

ates ond

ned

eed-

air

sampler and also by means of "settle plates" containing trypticase soy agar with added blood. One or more colonies were later transferred from the agar to trypticase soy slants. These were incubated for 48 hours and then refrigerated.

TABLE II. SOURCE OF MATERIAL STUDIED (1,222 CULTURES)

The second of Marian Closes (1,000 Continue)	
Physicians	
Obstetricians	17
Pediatricians	7
House staff	
Obstetricians	5
Pediatricians	5 2
r ediatricians	2
Graduate nurses	
Obstetric	31
Pediatric	10
Student nurses	
Obstetric	15
Pediatric	11
Mothers	
Ward	53
Private	53
Frivate	99
Babies	
Ward	53
Private	53
***************************************	
Fathers	
Ward	23
Private	29
Auxiliary personnel	17

The cultures thus obtained were gram-stained and then tested for the ability to clot human plasma. Coagulase reactions were performed by using human plasma of known reactivity. These were read at 4 hours and, in doubtful instances, at 12 hours. All cultures showing any coagulase production were submitted for bacteriophage typing.

# Results

The results of our investigation are best detailed by a series of charts with a brief interpretation and description of the findings. Since phage-type 44A appeared so frequently, we have based our study on the presence of this strain. Table III, however, gives an analysis of bacteriophage types found.

TABLE III. ANALYSIS OF BACTERIOPHAGE TYPING\*

BACTERIOPHAGE GROUP	NO. OF ISOLATES IN GROUP	% OF ALL TYPEABLE STRAINS
I	14	3.0
II	6	1.5
III	45	10.5
Miscellaneous		
80/81	25	6.0
44A	338	79.0
Total	428	100.0

\*Total number of isolates, 672; nontypeable, 244; typeable, 428.

#### I. Cultures Taken in the Hospital.—

A. Nasal cultures of hospital personnel: Table IV outlines the nasal cultures taken from various hospital personnel. As is to be expected, the

highest incidence of coagulase-positive staphylococci and of type 44A occurred in residents and nurses, evidently because these individuals spend more time in the hospital and in direct patient care.

TABLE IV. NASAL CULTURES OF HOSPITAL PERSONNEL

	NO.	COAGULASE POSITIVE	TYPE 44A
Obstetricians	17	8	2
Pediatricians	7	5	2
Pediatric nurses	11	10	5
Obstetric nurses	15	13	3
Residents (obstetric and pediatric)	5	4	4
Student clerks	21	10	1
Auxiliary personnel	23	14	4

B. Nasal cultures of mothers at the time of admission: Fifty-one ward and 41 private patients were so cultured. The incidence of coagulase-positive staphylococci was 55 per cent and 49 per cent, respectively. Sixteen and 15 per cent, respectively, were type 44A (Table V). Possibly these people were colonized in the clinic and in the private physicians' offices.

TABLE V. NASAL CULTURES OF MOTHERS AT TIME OF PREPARATION

	ROOMING-IN	NURSERY
Cultures	51	41
Coagulase-positive	28 (55%)	20 (49%)
Type 44A	8 (16%)	6 (15%)

C. Vaginal cultures of mothers at time of admission: Forty-four ward and 38 private patients had vaginal cultures taken at the time of preparation for delivery. Thirty and 8 per cent, respectively, had coagulase-positive staphylococci; the incidence of type 44A was 6.8 per cent and 2.6 per cent (Table VI). Here again it is assumed that type 44A might have been contacted in the outpatient department and in the private offices from personnel carrying the organism.

TABLE VI. VAGINAL CULTURES OF MOTHERS ON ADMISSION

	ROOMING-IN	NURSERY
Cultures	44	38
Coagulase-positive	13 (30%)	3 (8%)
Type 44A	3 (6.8%)	1 (2.6%)

D. Breast milk cultures on the third postpartum day: The choice of breast versus bottle feeding in ward and private patients is shown in Table VII.

TABLE VII. BREAST MILK CULTURES ON THIRD DAY

	ROOMING-IN	NURSERY
Breast feeding	43 (81%)	15 (28%)
Bottle feeding	10 (19%)	38 (72%)
Cultures	42	33
Coagulase-positive	19 (45%)	13 (39%)
Type 44A	8 (19%)	8 (24%)

Eighty-one per cent of ward mothers and 28 per cent of private mothers nursed their babies. The percentage of type 44A in breast milk was slightly

in

d

d

d

l,

higher in private (24 per cent) than in ward patients (19 per cent) and was not correlated with nasal carriage of type 44A in the mother, or with breast feeding.

E. Nasal cultures of mothers at time of discharge: The average length of hospital stay of ward and private mothers varied; the former were hospitalized for 3 days post partum, the latter for 7 days. The incidence of coagulase-positive organisms was approximately the same in ward (54 per cent) as in private patients (59 per cent). There was a slightly higher frequency of type 44A in private (35 per cent) as compared with ward patients (25 per cent) (Table VIII). Both ward and private patients doubled the incidence of coagulase-positive staphylococci during their hospitalization.

TABLE VIII. NASAL CULTURES OF MOTHERS AT DISCHARGE

	ROOMING-IN	NURSERY
Average stay	3 days	7 days
Cultures	52	46
Coagulase-positive	28 (54%)	27 (59%)
Type 44A	13 (25%)	16 (35%)

F. Nasal cultures of infants at time of discharge: For purposes of the investigation, we have divided the infants into those that roomed-in (i.e., stayed at the mother's bedside more or less constantly after the first 24 hours and those that were cared for in the nursery (Table IX). It is to be noted that the incidence of coagulase-positive staphylococci in the infant nasal passages at the time of discharge was slightly higher in those infants that were cared for in the nursery. The incidence of type 44A was twice as high in infants tended in the nursery (76 per cent) as in those who roomed-in (36 per cent). This was determined to be a highly significant difference upon application of the chi-square test.

TABLE IX. NASAL CULTURES OF INFANTS AT DISCHARGE

	ROOMING-IN	NURSERY
Cultures	50	49
Coagulase-positive	37 (74%)	46 (94%)
Type 44A	18 (36%)	37 (76%)

G. Periumbilical skin cultures of infants at time of discharge: Table X indicates that nursery infants had a higher incidence (79 per cent) of coagulase-positive staphylococci on their skin than babies who roomed-in. As was the case with the nasal cultures, type 44A was twice as frequent in nursery (56 per cent) as in rooming-in babies (26 per cent). It should be mentioned, in connection with both nasal and skin cultures of the newborn, that babies who roomed-in were usually ward babies who were discharged in 3 days rather than the 6 or 7 days of private babies.

TABLE X. PERIUMBILICAL SKIN CULTURES OF INFANTS AT DISCHARGE

	ROOMING-IN	NURSERY
Cultures	50	49
Coagulase-positive	23 (46%)	39 (79%)
Type 44A	13 (26%)	26 (56%)

H. Fathers: Cultures were obtained from a total of 51 fathers, usually on the occasion of their first visit after the birth of the baby. Since no follow-up

cultures were obtained, it is impossible to determine if these organisms were transient or permanent residents. Table XI details in part the character of the organisms cultured.

TABLE XI. NASAL CULTURES OF FATHERS

	ROOMING-IN	NURSERY
Cultures	22	29
Coagulase-positive	9 (41%)	16 (55%)
Type 44A	3 (14%)	9 (31%

I. Fomites: Various and many fomites in the labor and delivery rooms, the ward and private nurseries, and the formula room were cultured. Staphylococci were frequently found. The "epidemic" strain (44A), however, was cultured most frequently from the private nurseries.

# II. Cultures Taken in the Home .-

A. Follow-up of mothers and infants in the home: A follow-up of mothers and babies, from both the ward and the private service, in the home at 10 to 12 weeks post partum was possible with the help of a group of senior medical students. Nasal cultures were taken from both the mother and the infant (Tables XII and XIII).

TABLE XII. NASAL CULTURES OF MOTHERS AT FOLLOW-UP, 10 WEEKS AFTER DISCHARGE

	ROOMING-IN	NURSERY
Cultures	33	42
Coagulase-positive	23 (70%)	27 (64%)
Type 44A	10 (30%)	16 (38%)

TABLE XIII. NASAL CULTURES OF INFANTS AT FOLLOW-UP, 10 WEEKS AFTER DISCHARGE

	ROOMING-IN	NURSERY
Cultures	34	43
Coagulase-positive	27 (79%)	36 (84%)
Type 44A	14 (41%)	30 (69%)

The incidence of coagulase-positive and type 44A staphylococci in the maternal nasal passages remained approximately the same as at the time of discharge. There was a slight decrease both in coagulase-positive staphylococci in the nasal passages of the infants and in the incidence of type 44A. Neither decrease, however, was marked.

B. Specific infections during the course of the study: Four infections developed among patients during the course of the study, one of which was a postpartum breast abscess in a ward mother from whom Staphylococcus aureus, type 44A, was cultured. The other 3 occurred in babies cared for in the private central nursery. These included an auxiliary abscess, type 44A, which developed 3 days after birth; a cervical lymphadenitis, and a breast abscess, both in male infants, from whom no cultures were obtained.

# Comment and Summary

It is not our intent to review the subject of staphylococci in obstetric and nursery units. Many excellent reviews and studies have appeared. 6-11 Relatively little has been written concerning rooming-in versus nursery care.

1233

although an extensive experience at our own institution<sup>12</sup> has certainly suggested that babies isolated at the bedside have fewer infections than those cared for in the nursery. Ravenholt13 has also recommended rooming-in.

It is commonly accepted that shorter hospital stay is conducive to less staphylococci colonization. This is confirmed in obstetric patients by the work of Murray.14

The particular phage-type most frequently isolated in this study was type 44A. This is somewhat at variance with the predominant type found by Wise and associates<sup>15</sup> in our surgical operating rooms. Whether this is significant or not we cannot say. That phage-type 44A was isolated in some instances from maternal nasal and vaginal cultures on admission is somewhat surprising although Sarason<sup>2</sup> has reported that about 6 per cent of prenatal patients harbor penicillin-resistant staphylococci in the nose.

#### Conclusions

It cannot be said whether rooming-in or early discharge was responsible for the difference in colonization of babies with coagulase-positive staphyloeocci, type 44A.

The study suggests, however, that the safest procedure from the viewpoint of preventing infection is to isolate the baby with the mother and to discharge both mother and baby as soon as possible.

Many individuals have helped in the implementation of the study and the authors wish to thank the following persons: Hans Keitel, M.D. (Professor of Pediatries); Anita Fink, R.N.; Marian Bervinchak, R.N.; Jean LaLiberte, B.S., R.N.; Julian Feldman, M.D.; Vernon Wong, M.D.; Paul Flicker, M.D.; Norman Jablon, M.D.; Robert Kalish, B.S.; B. C. Lucas, M.S. (Department of Public Health, Philadelphia); and the residents of the Department of Obstetrics and Gynecology.

#### References

- Breed, R. S., Murray, E. G. D., and Smith, N. R., editors: Bergey's Manual of Determinative Bacteriology, Baltimore, Md., 1957, Williams & Wilkins Company.
   Sarason, E. L., and Bauman, S.: Surg. Gynec. & Obst. 105: 224, 1957.
- 3. Demerec, M.: J. Bact. 56: 63, 1948.
- Zebovitz, E., Evans, J. B., and Niven, C. F.: J. Bact. 70: 686, 1955.
   Lang, W. R.: Philadelphia Med. 49: 455, 1953.

- Rountree, P. M., and Barbour, R. G. H.: M. J. Australia 1: 525, 1950.
   Barber, M., Wilson, B. D. R., Rippon, J. E., and Williams, R. E. O.: J. Obst. & Gynaec. Brit. Emp. 60: 476, 1953.
- Colbeck, J. C.: Canad. M. A. J. 61: 557, 1949.
   Shaffer, T. E., Baldwin, J. N., Rheins, M. S., and Sylvester, R. F.: Pediatrics 18: 750, 9. Shaffer,
- Wysham, D. N., et al.: New England J. Med. 257: 295, 1957.
   Cook, J., Parrish, J. A., and Shooter, R. A.: Brit. M. J. 1: 74, 1958.
- 12. Montgomery, T. L., Steward, R. E., and Shenk, E. P.: Am. J. Obst. & Gynec. 57: 176,
- 13. Ravenholt, R. T., and Ravenholt, O. H.: Am. J. Pub. Health 48: 277, 1958.
- Murray, W. A., Jr., McDaniel, G. E., and Reed, M.: Am. J. Pub. Health. 48: 310, 1958.
   Wise, R. I., Sweeney, F. J., Haupt, G. J., and Waddell, M. A.: Ann. Surg. 149: 30,

# PRESENTATION AND PROLAPSE OF THE UMBILICAL CORD

L. M. Norburn, M.B., Ch.B., M.R.C.O.G., Northampton, England

Para

Para Para

Para Para

Para

Tota

(From St. Mary's Hospitals, Manchester, England)

OVER 100 years ago James Stephens¹ wrote, "The fatal results, as regards the life of the child, so frequently observed when the cord descends during labor, renders it very desirable to endeavour to lessen the excessive mortality shown in the records of the profession." These words would still appear to be true today, when the fetal mortality is authoritatively quoted as varying from 50 to 60 per cent.<sup>5</sup>

It is the purpose of this paper to investigate those cases in which prolapse of the fetal umbilical cord occurred and to attempt to learn how the related fetal perinatal mortality may be further reduced. The material for this paper has been obtained from a study of all the cases of prolapse or presentation of the cord occurring in Saint Mary's Hospitals during the 5 year period, 1951 to 1955. This quinquennium is later compared with the corresponding period 20 years earlier.

#### Incidence

Presentation or prolapse of the cord occurred 84 times in 16,487 consecutive deliveries from 1951 to 1955 at St. Mary's Hospitals, a total incidence of 0.51 per cent or 1 in 196. The incidence in "booked" cases was 0.43 per cent or 1 in 232, while in "emergency" cases it was 1.12 per cent or 1 in 89. The emergency cases accounted for 24 per cent of the total admissions.

A total of 1,031 fetal perinatal deaths occurred during this period and of these, 2.9 per cent or 1 in 34 were related to presentation or prolapse of the cord.

Table I shows the incidence of prolapse of the cord in relation to maternal age and parity. Let us exclude for the moment the very young nulliparous group where the high incidence of prolapse of the cord is related to the high frequency of prematurity (60 per cent). It is now seen that the risk of cord prolapse increases as either maternal age or parity increases. However, the greatest risk of cord prolapse at each parity changes from the oldest age group in the nulliparous patients to the youngest age group in the grand multiparous patients. This very high risk (1 in 21) in the youngest age group of the grand multiparas demonstrates one of the various disadvantages associated with the too frequent recurrence of pregnancy.

## **Etiological Factors**

The incidence of the various etiological factors for the 5 year period is shown in Table II. The factors, of course, may be multiple in any one case.

a

TABLE I. INCIDENCE OF PROLAPSE OF THE CORD IN RELATION TO AGE AND PARITY

				AGE (YEARS)			
	UNDER 20	20-24	25-29	30-34	35-39	OVER 40	TOTAL
Para 0	5 in 414 (1 in 83)	6 in 2074 (1 in 346)	4 in 1865 (1 in 466)	5 in 1024 (1 in 205)	2 in 555 (1 in 277)	1 in 195 (1 in 195)	23 in 6127 (1 in 266)
Para i	0 in 46	3 in 512 (1 in 171)	4 in 914 (1 in 228)	4 in 751 (1 in 188)	5 in 479 (1 in 96)	4 in 166 (1 in 41)	20 in 2868 (1 in 143)
Para ii	0 in 4	1 in 117 (1 in 117)	3 in 398 (1 in 133)	4 in 401 (1 in 100)	5 in 291 (1 in 58)	1 in 104 (1 in 104)	14 in 1315 (1 in 94)
Para iii	0 in 1	0 in 23	1 in 132 (1 in 132)	6 in 200 (1 in 33)	3 in 140 (1 in 47)	0 in 77	10 in 573 (1 in 57)
Para iv	0 in 0	0 in 1	1 in 56 (1 in 56)	2 in 93 (1 in 46)	1 in 105 (1 in 105)	0 in 43	4 in 298 (1 in 74)
Para v and over	0 in 0	0 in 4	0 in 39	6 in 128 (1 in 21)	4 in 169 (1 in 42)	3 in 130 (1 in 43)	13 in 440 (1 in 34)
Total	5 in 465 (1 in 93)	10 in 2731 (1 in 273)	13 in 3404 (1 in 262)	27 in 2597 (1 in 96)	20 in 1739 (1 in 87)	9 in 715 (1 in 79)	

Malpresentation was by far the commonest single predisposing factor. Prolapse of the cord occurred only once in every 379 cases of vertex presentation, but when the fetal presenting part fitted the lower segment of the uterus less accurately, the incidence rose markedly to 1 in 59 with face presentation, 1 in 30 with breech presentation, and 1 in 6 with transverse lie or compound presentation.

It is interesting to see how infrequently prolapse of the cord is predisposed to by pelvic contraction or placenta previa, but, as will be seen later, their importance in relation to fetal perinatal mortality far outweighs their etiological frequency.

TABLE II. INCIDENCE OF ETIOLOGICAL FACTORS

ETIOLOGICAL FACTORS	NO.	INCIDENCE (%)
Malpresentation	43	51.2
Prematurity (< 5½ pounds)	32	38.1
Multiple pregnancy	19	23.6
Grand multipara (Para v+)	13	15.5
High mobile head when membranes ruptured	13	15.5
Hydramnios	8	9.5
Placenta previa	7	8.3
Fetal abnormality	7	8.3
Contracted pelvis	6	7.1
Obstetrical manipulations	5	5.9
Obliquity of uterus	1	1.1
Vomiting under anesthesia	1	1.1
Unknown	5	5.9

Five cases of prolapse of the cord occurred during the course of obstetrical manipulations. Two of these occurred during vaginal manipulations at the time of attempted forceps delivery (one of them before admission to hospital); one followed artificial rupture of the forewaters in the presence of a high and mobile head; another occurred when labor was induced with a hydrostatic bag which displaced the presenting part and allowed the cord to prolapse; and the other was a case of transverse lie with ruptured forewaters which was treated by internal version followed by plugging the cervix with the half breech, but it was discovered later that this trapped the cord between the cervix and breech.

# Diagnosis

Prolapse of the cord was diagnosed on 84 occasions, and on 28 of these (33.3 per cent) the diagnosis was made only when the cord presented at the

vulva. After excluding the 6 cases in which the child was delivered almost immediately after discovery of the cord at the vulva, the corrected perinatal mortality was 23.5 per cent. This compares satisfactorily with the corrected perinatal mortality of 25 per cent for all cases. It is therefore doubtful if spasm of the cord vessels plays such an important role in causing fetal death as has been suggested since presumably the vascular spasm would be most marked in those cords which prolapse outside the vulva.

In the remaining cases, the prolapsed cord was found on digital pelvic examination, but in only 12 cases (14.3 per cent) was the vaginal examination performed for fetal distress. Most commonly (47.6 per cent of all cases) the prolapsed cord was found during routine vaginal examination with the possibility in mind; following spontaneous rupture of the membranes (20 cases); while the course of labor was being assessed (14 cases); or following delivery of the first of twins (6 cases). In 4 cases (4.8 per cent) the prolapsed cord was found during vaginal manipulations.

# Prognosis

- A. Maternal Mortality.—There were no maternal deaths associated with prolapse of the cord during the period under review.
- B. Fetal Perinatal Mortality.—There were 30 fetal perinatal deaths due to prolapse of the cord from 1951 to 1955, giving a perinatal mortality rate of 1.9 per 1,000 deliveries.

The value of antenatal care even in this obstetrical emergency is seen when the fetal perinatal mortality for booked cases is found to be 32.3 per cent while that for the emergency cases is 47.4 per cent.

Examination of Table III will show how the corrected fetal perinatal mortality of 25 per cent has been obtained from a gross perinatal mortality of 35.7 per cent. It will be noted that the correction has been made only in order to obtain the perinatal mortality for "treatable" cases. The treatable cases are those cases in which the fetus is alive and normal when the patient is admitted to hospital. No correction has been made for prematurity, except in so far as all the cases were at or past the twenty-eighth week of gestation.

TABLE III. CORRECTED FETAL PERINATAL MORTALITY

		NO.	FETAL MORTALITY
Total cases of prolapse of cord		84	
Number of perinatal deaths		30	35.7
Less fetal abnormalities			
incompatible with life	7		
Less babies dead on admission			
but otherwise normal	5		
Remaining perinatal deaths		18	25.0
Total babies normal and alive on adm	ission	72	

In the following analysis only treatable cases have been considered.

Presentation of the cord was found on 10 occasions. This precursor of the prolapsed cord caused 2 fetal deaths before the membranes ruptured. Three of the 8 remaining patients were rapidly and easily delivered vaginally after rupture of the forewaters, while 5 were delivered by cesarean section. It will therefore be seen that at Saint Mary's Hospitals presentation of the cord is considered to be almost as serious for the fetus as true prolapse of the cord and is certainly not regarded so complacently as it is in most text-books.

# Important Factors in Relation to Fetal Perinatal Mortality.—

1. Degree of cervical dilatation: This is a very important factor in relation to the fetal perinatal mortality, as can be seen from Table IV.

TABLE IV. DEGREE OF CERVICAL DILATATION

	CASES		FETAL MORTALITY		
DILATATION OF CERVIX WHEN PROLAPSE DIAGNOSED	NO.	INCIDENCE (%)	NO.	INCIDENCE (%)	
Fully dilated	40	55.6	7	17.5	
34 dilated	4	5.6	2	50.0	
1/2 dilated	9	12.5	6	66.7	
1/4 dilated	19	26.4	3	15.8	

When the cervix is fully dilated, the fetus can usually be rapidly, easily, and safely delivered vaginally, but, with an incompletely dilated cervix, immediate vaginal delivery is appreciably more difficult; there is a much greater risk of fetal death, and replacement of the cord also carries a high fetal mortality. The perinatal mortality, therefore, falls sharply as the cervical dilatation increases. When the cervix was only slightly dilated, however, the perinatal mortality was markedly diminished, and the fetal survival rate was better than with the fully dilated cervix. This was due to the frequent use of abdominal delivery in this type of case. It is noteworthy that all the 16 living children obtained from those cases where the cervix was only slightly dilated were delivered by cesarean section.

2. Fetal maturity: Table V reveals the importance of fetal maturity in relation to the perinatal mortality from prolapse of the cord. The premature baby, as always, is adversely affected by any complication of labor.

TABLE V. FETAL MATURITY

		FETAL MORTALITY			
	CASES	NO.	INCIDENCE (%)		
Mature normal babies	47	10	21.3		
Premature normal babies (< 5½ pounds)	25	8	32.0		

3. Fetal presentation: It is surprising to find on referring to Table VI that the perinatal mortality was not appreciably influenced by the fetal presentation. This was at least partly related to the leveling influence of cesarean sections, as can be seen by excluding the cases of cesarean section thereby causing the perinatal mortality for breech presentation to be 25 per cent while for vertex presentation it is 32 per cent. This confirms the contention of Bourgeois<sup>3</sup> that the irregular soft breech is less liable to compress the cord than the harder rounded vertex presentation, provided the child is delivered vaginally.

TABLE VI. FETAL PRESENTATION

	CASES	FETAL MORTALITY			
		NO.	INCIDENCE (%)		
Vertex	37	9	24.3		
Breech	18	4	22.2		
Transverse or compound	16	4	25.0		
Face	1	1	100.0		

The perinatal mortality for transverse or compound presentations, even after the cases of cesarean section are excluded, was still only 34 per cent

because almost half the cases occurred in the second of twins. When those cases relating to the second of twins were excluded, it was found that of the 7 remaining treatable infants who were delivered vaginally 4 died.

- 4. Contracted pelvis: Three fetal perinatal deaths occurred in the 6 cases of pelvic contraction in which the cord prolapsed. This high fetal loss was due to the fact that attempted vaginal delivery was more difficult than had been anticipated. The 3 living children were all delivered by cesarean section.
- 5. Multiple pregnancy: The risk of cord prolapse was markedly increased in multiple pregnancy, especially for the first child. The first child's cord prolapsed once in every 24 cases of multiple pregnancy, whereas the risk for the second child was 1 in 41. The cord of the first child prolapsed on 11 occasions, with a 27.3 per cent perinatal mortality. The second child's cord prolapsed on 7 occasions but there were no fetal deaths. These mortality figures agree with those of Fenton and D'Esopo<sup>2</sup> and are, of course, accounted for by the fact that prolapse of the second child's cord occurs under ideal circumstances.
- 6. Placenta previa: Five treatable cases of placenta previa associated with prolapse of the cord occurred, and 2 of the cases had a low insertion of the cord. Three of the 5 mothers were delivered of living children by cesarean section; of the 2 delivered vaginally, 1 died.
- 7. Fetal abnormality: In this series of cases, 8.3 per cent of the babies had abnormalities incompatible with life. Therefore, before a cesarean section is performed for prolapse of the cord, careful clinical examination should always be carried out to exclude the common fetal abnormalities of anencephaly and hydrocephaly.

#### Treatment

Initial Treatment.—Postural or digital elevation of the presenting part to relieve the pressure on the prolapsed cord is frequently advised as an interim measure while the institution of more radical methods of treatment is awaited. Elevation of the presenting part was specifically mentioned only 14 times in the case records, but I feel sure it was used far more frequently. This initial therapy would appear to be effective since no child was lost during the waiting period and all the cases of fetal distress improved, except one, which occurred in a grand multipara having strong uterine contractions, who waited 1½ hours for a cesarean section to be carried out. On this occasion obviously too much was demanded of this initial method of treatment.

Active Treatment.—Table VII depicts the various methods utilized in the delivery of the treatable cases of prolapse of the cord at Saint Mary's Hospitals from 1951 to 1955, together with the incidence and perinatal fetal mortality associated with each method.

Those patients in whom the prolapsed cord was diagnosed at full cervical dilatation were all delivered vaginally and are marked by an asterisk (\*) in Table VII. In this type of case the average perinatal mortality rate was 17.5 per cent. Analysis of the 7 perinatal deaths which occurred shows that 2 were associated with contracted pelves which caused difficulty in forceps delivery, resulting in fetal death from asphyxia; 2 of the fetal deaths were associated with delay in the institution of treatment; 2 other deaths occurred in markedly premature babies (2 pounds, 2 ounces, and 3 pounds, 4 ounces), and one fetal asphyxial death occurred despite an apparently rapid and easy forceps delivery. It would therefore appear that still further improvement in the fetal survival rate could have been obtained in this group of cases by immediately proceeding with rapid vaginal delivery, provided this was reasonably easy; but in those cases complicated by pelvic contraction a rapid cesarean section holds out the best chance of fetal survival.

9

e

e n

d o- e s, d e e t

h ie n

d is s d

n

1.

nal

e-d y

1e

Is

V

al

in

.5

re

v.

1.

al

e-

al

1.

ıt

TABLE VII. METHODS OF DELIVERY

		1951 т	0 195	5		1931 т	o 193	5
	CA	CASES MORTALITY CASES		SES	FETAL MORTALITY			
	NO.	1 %	NO.	1 %	NO.	1 %	NO.	1 %
Cesarean section	18	25	1	5.6	4	9.5	0	0
Forceps delivery*	22	30.6	5	22.7	8	19.0	3	37.5
Forceps delivery through incompletely								
dilated cervix†	1	1.4	0	0	_		-	-
Assisted breech delivery*	3	4.2	0	0	-	-	-	-
Breech extraction*	8	11.1	0	0	7	16.7	1	14.3
Breech extraction through incompletely								
dilated cervix†	5	6.9	2	40.0	3	7.1	2	66.7
Internal version and breech extraction*	3	4.2	0	0	2	4.8	2	100.0
Cord replacement, internal or bipolar version, cervix plugged with ½ breech, then breech extraction through incom-	3	4.2	3	100	3	7.1	1	33.3
pletely dilated cervix† Cord replacement; internal or bipolar version, and cervix plugged with ½								
breecht	1	1.4	1	100	3	7.1	3	100
Cord replacement and cervix plugged with ½ breech†	1	1.4	1	100	1	2.4	1	100
Cord replacement and bipolar cephalic version†		-	_		1	2.4	0	0
Cord replacement	1	1.4	1	100	1	2.4	1	100
Internal version and high forceps*					1	2.4	1	100
Failed forceps, later craniotomyt	-	-	-		2	4.8	2	100
Intrauterine death after admission, later craniotomy					1	2.4	1	100
Intrauterine death after admission.					1	6.1	1	100
later delivery by natural forces	2	2.8	2	100	3	7.1	3	100
Vertex delivery by natural forces*	4	5.6	2	50	2	4.8	1	50.0
Total	72	0.0	18	00	42	110	22	0010

\*Patients delivered vaginally at full cervical dilatation. (See text.)

†Cases treated by vaginal manipulation when prolapsed cord was diagnosed at incomplete cervical dilatation. (See text.)

Those patients treated by vaginal manipulations when the prolapsed cord was diagnosed in association with an incompletely dilated cervix and a living fetus are marked by a dagger (†) in Table VII. The average perinatal mortality for these cases was 67 per cent. It is in this group of cases that most improvement in the perinatal survival rate is to be looked for in the future, by more frequent recourse to cesarean section.

The vaginal manipulations utilized in these cases with incomplete dilatation of the cervix were either vaginal delivery through the undilated cervix or replacement of the cord or a combination of both.

Vaginal delivery through an incompletely dilated cervix was performed for prolapse of the cord on 9 occasions with 5 perinatal deaths. All these perinatal deaths were related to breech extraction through an undilated cervix although in 2 cases there was also marked prematurity. This method of treatment, therefore, carried with it the high fetal perinatal mortality of 56 per cent. The very definite risk of damage to the mother by this treatment is emphasized when it is found that the maternal genital infection rate in these cases is  $3\frac{1}{2}$  times that for all the other cases of prolapsed cord.

Replacement of the prolapsed cord was attempted on 6 occasions. It succeeded in 4 cases but failed in 1, and the prolapse recurred in another case. All the babies died, but in 3 the immediate cause of death was breech extraction through an undilated cervix undertaken because of fetal distress.

It is unfortunate that manual replacement of the prolapsed cord, which is such an eminently reasonable method of treatment, carries such a poor

chance of fetal survival. In the cases under review, cotton gauze was utilized in the replacement, but it is doubtful if the cord was always fully replaced above both the presenting part and the retraction ring, into the upper segment of the uterine cavity. Probably the cord had not been fully replaced in those cases where the prolapse recurred, or fetal distress developed shortly after apparently successful reposition. Perhaps it is technically too difficult to replace the cord on every occasion completely into the upper uterine segment, especially for the junior obstetrician, who nowadays has less opportunity of performing difficult vaginal maneuvers, but who may suddenly be called upon to deal with this emergency.

It may be of interest to here record a case which occurred in 1954, when a fetus whose heart became inaudible and whose cord had ceased to beat was delivered alive. At routine examination of a multiparous patient in labor, the fetal heart sounds suddenly ceased. Vaginal examination revealed a fully dilated cervix through which was protruding a nonpulsatile cord. A rapid and easy midcavity forceps delivery resulted in the birth of a living healthy

child.

# Comparison With 1931 to 1935

Prolapse of the cord occurred on 64 occasions from 1931 to 1935, giving an incidence in "booked" cases of 1 in 201 and in "emergency" cases of 1 in 73. Just over half of the cases were emergency admissions and many of the babies were already dead on admission, leaving 42 "treatable" cases. The corrected fetal perinatal mortality for the treatable cases was 52.4 per cent, which is rather more than double the corresponding figure for 1951 to 1955.

If we consider how this fetal perinatal mortality has been lowered over the 20 year interval, it may point the way to a further reduction of the

perinatal mortality in the future.

In Table VII are listed methods utilized for the delivery of treatable cases of prolapse of the cord during 1931 to 1935 as well as the associated

fetal perinatal mortality rates.

Those patients delivered vaginally at full cervical dilatation during 1931 to 1935 are marked by an asterisk (\*) in Table VII. If we compare these cases with the similar cases occurring during 1951 to 1955 it will be seen that the incidence of the cases is the same but the perinatal mortality for 1931 to 1935 was 40 per cent while during the period 1951 to 1955 it was 17.5 per cent. This fall in perinatal mortality during the 20 year interval is mainly related to a change in etiology, especially in regard to pelvic contraction, with which 20 per cent of the cases of prolapsed cord were associated from 1931 to 1935, almost treble the incidence from 1951 to 1955. In those patients delivered vaginally at full cervical dilatation from 1931 to 1935, 4 of the 8 perinatal deaths were associated with pelvic contraction. This again emphasizes the need to carefully exclude pelvic contraction before embarking on vaginal delivery for prolapse of the cord.

Those cases treated by vaginal manipulations during 1931 to 1935 when the prolapsed cord was diagnosed at incomplete cervical dilatation, are designated by a dagger (†) in Table VII. When these cases are compared with the similar cases occurring during the later quinquennium, it is seen that the perinatal mortality has remained very close to 70 per cent, but the incidence of these cases has decreased from 33.3 per cent in 1931 to 1935 to 16.7 per cent in 1951 to 1955. This fall in incidence of vaginal delivery has, of course, been accompanied by a parallel increase in the cesarean section rate during the 20 year interval, which has resulted in halving the perinatal mortality for all those cases of prolapsed cord diagnosed at incomplete cervical dilatation. This undoubtedly indicates one of the main paths we may follow in order to

save the lives of more babies in the future.

e e r

Another important factor has also tended to produce a general elevation of the fetal perinatal mortality rate for 1931 to 1935. Fifty-three per cent of the patients admitted during this period were emergency cases, and many of them were in poor general condition. Indeed 16 of these babies were already dead and 2 of the mothers died from shock and infection shortly after admission. Presumably an appreciable number of the babies, although alive on admission, were not fit to stand more than the easiest of deliveries. I feel sure this factor contributed to a general elevation of the fetal mortality during the period 1931 to 1935, but to what extent I am unable to ascertain from the notes.

The incidence of the cases diagnosed at each level of cervical dilatation has remained remarkably constant during both 5 year periods and therefore this factor has had no influence on the changed perinatal mortality.

#### Comment

It is apparent from what has been said above that if the fetal perinatal survival rate is to be further increased, continuous vigilance must be exercised with the possibility of prolapse of the cord ever at the back of one's mind, and should the possibility materialize, then, in the main, only 2 lines of treatment should be followed: (1) immediate vaginal delivery, provided the cervix is fully or almost fully dilated and delivery is expected to be easy; (2) immediate cesarean section if the cervix is incompletely dilated or vaginal delivery is expected to be difficult for any other reason, such as pelvic contraction.

I would like to plead that the full equipment for a cesarean section should always be kept sterilized and ready for immediate use should such an emergency as prolapse of the cord arise. The cesarean section could, however, be performed in the labor ward if the operating theater were engaged. It is, of course, important to continue with the initial treatment while preparations are being made for the operation and to auscultate the fetal heart again immediately before the operation.

The objection to further increasing the cesarean section rate lies in the risk to the mother. Marshall and Cox<sup>6</sup> have shown that during the first 24 hours of labor the maternal risk is less than 0.35 per cent, and it is within this time limit that all cases of prolapsed cord were diagnosed at Saint Mary's Hospitals during 1951 to 1955 (except for 2 cases in each of which the baby weighed less than 3 pounds). Most mothers would, I feel sure, gladly accept this small risk in order to obtain a living child. Obviously if the risk to the mother from cesarean section is markedly increased, or the fetus has a poor chance of survival, an alternative method of treatment should be adopted, provided this carries a lower maternal risk.

The alternative courses of action are:

- 1. Replacement of the cord, which carries a high fetal perinatal mortality, and its usefulness is therefore restricted to those cases in which the chance of fetal survival is already doubtful, as in the case of marked prematurity.
- 2. Vaginal delivery through the undilated cervix or after manual dilatation of the cervix, which is associated with a high perinatal mortality and the risk of serious damage to the mother. The place of this treatment in modern obstetrical practice can be taken more safely by cesarean section.
- 3. An expectant policy is, of course, followed if the fetus is dead, or, very occasionally, in the treatable case when the maternal condition is so unsatisfactory (e.g., cardiac failure) that replacement of the cord under general anesthesia carries a maternal risk out of proportion to the poor chance of fetal survival.

# Summary

An analysis is presented of 84 cases of prolapse of the cord occurring from 1951 to 1955 at Saint Mary's Hospitals, and these have later been compared with the 64 cases which occurred during 1931 to 1935.

The incidence including the relationship to maternal age and parity has been considered.

Malpresentation and prematurity were the most common etiological factors.

The diagnosis has been discussed.

It is doubted if spasm of the cord vessels plays such an important role in causing fetal death as has been suggested elsewhere.

The corrected fetal perinatal mortality for 1951 to 1955 was 25 per cent.

Presentation of the cord carries a similar fetal risk to prolapse of the cord.

Certain important factors in relation to perinatal mortality have been considered.

The treatment, both initial and active, has been discussed and conclusions drawn as to how further reductions may be made in fetal perinatal mortality.

All the babies died when replacement of the cord was performed.

Immediate vaginal delivery through the incompletely dilated cervix carried a perinatal mortality of 56 per cent together with a high maternal morbidity rate.

It would appear that the fetal perinatal mortality may be further lowered by following 2 main lines of treatment, either immediate vaginal delivery, if this is easy, or immediate cesarean section.

All treatable cases, except in 2 markedly premature infants, of prolapse of the cord at Saint Mary's Hospitals from 1951 to 1955 occurred within the first 24 hours of labor, when the maternal risk from cesarean section is low.

I wish to express my thanks to the chairman and members of the Medical Committee of Saint Mary's Hospitals for permission to quote from the Hospital Records. I am also greatly indebted to Professor W. I. C. Morris for his invaluable help and criticism throughout the preparation of this paper.

#### References

- Stephens, J.: Lancet 2: 196, 1847.
   Fenton, A. N., and D'Esopo, D. A.: AM. J. OBST. & GYNEC. 62: 52, 1951.

- renton, A. N., and D'Esopo, D. A.: AM. J. OBST. & GYNEC. 62: 52, 1951.
   Bourgeois, G. A.: AM. J. OBST. & GYNEC. 41: 837, 1941.
   Rhodes, P.: Proc. Roy. Soc. Med. 49: 937, 1956.
   Moir, J. Chassar: Munro Kerr's Operative Obstetrics, ed. 6, London, 1956, Baillière, Tindall & Cox, p. 262.
   Marshall, C. M., and Cox, L. W.: Tr. Brit. Cong. Obst. & Gynaec. 12: 30, 1950.

# DEMONSTRATION OF CYTOMEGALIC INCLUSIONS IN AUTOLYZED FETAL TISSUE

LESTER F. BELTER, M.D., AND MARTA CAMILO, M.D., RICHMOND, VA.

(From the Department of Pathology, Medical College of Virginia)

RARE though it may be, any help that the pathologist can give the obstetrician in the determination of the cause of death of the macerated fetus is worthwhile, and the following account of the value of the autopsy examination of an apparently autolyzed fetus will illustrate the point.

## Case Report

Maternal History.—The mother was a 19-year-old white woman, gravida i, para 0, whose last menstrual period was Dec. 23, 1954. The expected date of confinement was Sept. 30, 1955. The patient's pregnancy appeared to progress normally until Sept. 5, 1955, at which time she began to have pain in the right costovertebral angle. The pain was intermittent with about 20 minute periods of duration. The character and nature of the pain were not described. Later, the pain became persistent and radiated around to the suprapubic region, being confined to the right side. The remainder of the history was noncontributory.

Physical examination at that time revealed a blood pressure of 130/70, pulse 85, respirations 20, temperature not elevated. Urine examination revealed one plus albuminuria and many white blood cells. The white cell count was 11,400 with 80 per cent neutrophils and 20 per cent lymphocytes. The fetus was viable at that time.

The patient was hospitalized and treated with Gantrisin. She responded satisfactorily, and was discharged 2 days later. On September 17 she was seen in the physician's office and at that time the baby's heartbeat was present. The following day the patient did not feel movement. On September 20 she went into labor and was delivered of a macerated fetus after a 4 hour, 42 minute labor.

Autopsy.—The autopsy performed 31 hours after delivery revealed a 2,100 gram, 46 cm. female infant partially covered with greenish-yellow stained skin which could easily be separated at the dermis. Large areas were already denuded on the abdomen and extremities. The body contour was flattened from loss of turgor. The subcutaneous tissues were watery and brownish-red. The abdominal and pleural cavities contained red-tinged fluid. All the viscera had the same red color. The organs showed no gross abnormalities of position and no malformation. On section they were soft and the fine details were not recognizable. The brain was liquefied. The gross diagnosis was third degree macerated fetus.

Microscopic sections were made from the heart, lungs, thymus, salivary gland, spleen, liver, gall bladder, adrenals, kidneys, umbilicus, and skin. These revealed severe autolysis with only fragments of cells being visible in the spleen, liver, kidneys, adrenals, gall bladder, and salivary gland. The lungs and thymus were reasonably well preserved. The liver showed only granular fragments of cells (Fig. 1) with all of the cells of the bile ducts being autolyzed. A few bile duct cells could be outlined and these contained large indistinctly visualized cytomegalic inclusions. The salivary gland (Fig. 2) revealed a similar pattern. The kidney

showed a loss of most of the epithelial elements; however, it was severely affected by the disease process with the affected tubules being clearly recognizable with a scanning lens. The intranuclear inclusions were remarkably well preserved (Fig. 3). The cytoplasmic

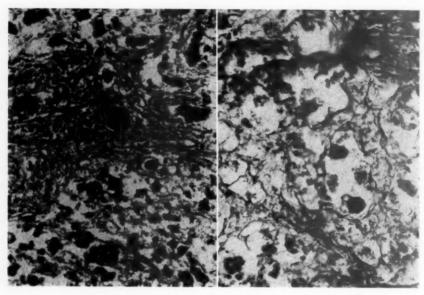


Fig. 1.

Fig. 2.

Fig. 1.—Liver showing bile duct epithelial cells with cytomegalic inclusion. Fragments of cells may represent erythropoietic elements. (Hematoxylin and eosin.  $\times 520$ ; reduced  $\frac{1}{16}$ .)

Fig. 2.—Salivary gland with almost total autolysis. Note large inclusion in preserved cell. (Hematoxylin and eosin.  $\times 520$ ; reduced  $\frac{1}{3}$ .)

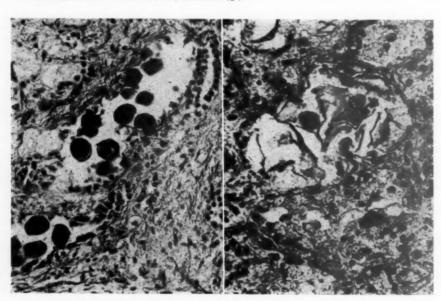


Fig. 3

Fig. 4

Fig. 3.—Section of kidney showing the preservation of the cells involved by cytomegalic inclusions. (Hematoxylln and eosin.  $\times 520$ ; reduced  $\frac{1}{2}$ .)

Fig. 4.—Alveolus filled with aspirated squamous epithelial cells and one cell containing cytomegalic inclusion. (Hematoxylin and eosin.  $\times 520$ ; reduced  $\frac{1}{2}$ .)

basophilic granules suggested the presence of the cytoplasmic form of the inclusions. The lungs showed large areas of aspirated cells from the amnionic fluid. Scattered throughout the lungs in small number were cells containing intranuclear inclusions (Fig. 4). From their distribution it was suggested that some, if not all, represented aspirated cells, probably of renal origin. The adrenals, heart, thymus, umbilicus, and skin were free of inclusions.

#### Comment

Cytomegalic inclusions were first described by Jesionek and Kiolemenoglou¹ and were clearly brought into focus as a cause of intrauterine and neonatal death by Cappell and McFarlane² and as a complicating disease of debilitated adults by Amromin.³

The virus, though similar to the salivary gland virus of rodents, appears to be species specific. It is of low virulence in animals and from the high incidence of apparently well adults (81 per cent) having a positive complement fixation test,<sup>4</sup> it would seem to have either a subclinical or an as yet unrecognized disease pattern in adults. There has been an insufficient number of cases in adults studied to give a clinical picture, as nearly all of the cases have been discovered at autopsy in which the patient died from some other cause, the disease usually being implanted on a fatal widespread neoplastic process.

Smith and Vellios,<sup>5</sup> in their comprehensive article, cite references to the presence of inclusions in the salivary glands of infants dying from all causes (up to 32 per cent), although the visceral organs are usually spared. In those cases presenting evidence of the disease, the clinical picture has been dominated by the hepatic involvement leading to jaundice, hepatomegaly, and splenomegaly, simulating erythroblastosis. In the older age infants and children, the clinical picture has largely been that of some type of pneumonia or enteritis. The inclusions are most commonly found in the kidney, lung, or liver, though nearly all organ systems have been cited at one time or another. In the newborn period the kidney has been involved in nearly all of the cases and the presence of cytomegalic inclusions within desquamated renal tubular cells in the urine led to the first antemortem diagnosis of the disease by Fetterman.6 In reviewing the literature, however, we, have been unable to find any evidence of a report of the persistence of the inclusions in autolyzed tissue in which nearly all cellular elements except the connective tissue framework and at least part of the affected cells were preserved.

It is not known whether the inclusions are resistant to autolytic enzymes or whether the cellular damage produced by the virus has resulted in the destruction of the normal autolytic enzymes or a marked reduction in their activity. A review of a number of other cases of cytomegalic inclusion disease in which there was a prominent neutrophilic reaction failed to reveal persistence of the involved cells to the exclusion of the unaffected cells.

The demonstration of the inclusions in the kidney almost universally in the fatal newborn or neonatal cases and the better state of preservation of the lungs in most autolyzed fetuses would seem to indicate that, if the gross organs are still recognizable as such, microscopic examination of at least the kidneys and lungs should be carried out in all cases of stillbirths or abortions.

### Summary

- 1. A case of a 2,100 gram, third degree, macerated fetus is reported in which cytomegalic inclusions were demonstrated in autolyzed tissue, demonstrating the persistence of the affected cells.
- 2. More careful examination of the lost products of conception is strongly urged to throw more light on a sadly neglected field.

# References

- Jesionek and Kiolemenoglou: Quoted by Cappell and McFarlane.<sup>2</sup>
   Cappell, D. F., and McFarlane, M. N.: J. Path. & Bact. 59: 385, 1947.
   Amromin, G.: A. M. A. Arch. Path. 56: 323, 1953.
   Rowe, W. P., Hartley, J. W., Waterman, S., Turner, H. C., and Huebner, R. J.: Proc. Soc. Exper. Biol. & Med. 92: 418, 1956.
   Smith, M. G., and Vellios, F.: A. M. A. Arch. Path. 50: 862, 1950.
   Fetterman, G. H.: Am. J. Clin. Path. 22: 424, 1952.

# MECONIUM PERITONITIS WITH ASCITES RESULTING IN DYSTOCIA

LEONARD A. WALL, M.D., KANSAS CITY, Mo.

M ECONIUM peritonitis is an aseptic chemical peritonitis caused by the entrance of meconium into the peritoneal cavity through a perforation in the intestinal tract during the late intrauterine or early neonatal period. In about one-half of the cases positive evidence of organic intestinal obstruction with perforation can be found, while in the other 50 per cent of cases no demonstrable obstruction or area of perforation can be found, indicating that many of the perforations probably close before birth.

The term "meconium peritonitis" is restricted to those cases in which meconium, calcified plaques, and usually foreign body giant cells are found in the peritoneum (Figs. 1 and 2).

Many of the cases reported in the literature show some degree of abdominal distension, mostly from gas with minor degrees of ascites, but seldom is the abdominal distention from ascitic fluid of sufficient degree to produce difficulty in delivery.<sup>1-3</sup> The following is a report of such a case.

History and Physical Examination.—The mother, a 23-year-old white gravida iii, para ii, was admitted to the hospital on July 29, 1956, in active labor. Her prenatal course had been entirely normal. She gave no history of past illnesses. Her previous pregnancies had ended normally with normal infants. Physical examination on admission revealed a pregnant white woman, near term, in active labor. The fetus was estimated to weigh 8 pounds, and was in the left occipitotransverse position at O station. The cervix was 7 cm. dilated. The fetal heart rate was 138 per minute and regular. The pelvis was clinically judged to be adequate. A short time after admission, the cervical dilatation had progressed to 9 cm., and the patient was taken to the delivery room in anticipation of a normal delivery.

Labor and Delivery.-The first stage of labor was promptly completed but the second stage was prolonged, requiring some 20 to 30 contractions to bring the head from O station to the perineal floor. When the head began to crown, a shallow midline episiotomy was made and the head was delivered with ease until the chin was ready to present. At this point moderate difficulty was encountered. It seemed the fetus would not descend sufficiently to allow the chin to deliver adequately. After the chin was delivered, an attempt was made to deliver the anterior shoulder with the next pain; however, this could not be accomplished. The posterior arm and shoulder were delivered with considerable difficulty and the fetus was rotated so that the anterior shoulder became posterior, and again difficulty was encountered in delivering the second arm and shoulder. Fracture of both clavicles was produced during delivery of the shoulders and arms. From this point it was impossible to complete the delivery even with strong traction and firm fundal pressure. The possibility of Siamese twins, or a tumor of the fetal abdomen or sacral region was entertained. Delivery to this point had been accomplished under pudendal block with nitrous oxide supplement. Portable x-ray examination revealed a single fetal skeleton with no abnormalities. No calcified or soft tumor masses could be identified.

With the patient now under general anesthesia, the operator's hand was placed up along the curve of the sacrum and it was ascertained that the abdomen of the fetus was markedly distended. By this time the infant had died and it was decided to decompress the abdominal distention by an incision into the abdomen with long scissors. Before this was done, a final attempt to deliver by means of strong traction and fundal pressure was tried and this time the female infant was delivered rather precipitously.

Immediately after delivery it was noted that a large quantity of straw-colored fluid was coming from the vagina of the infant. Further examination revealed a perforation in the cul-de-sac through which ascitic fluid had escaped in sufficient quantity to allow decompression of the abdomen and subsequent delivery.

A third degree extension of the midline episiotomy was repaired and the mother's postpartum course was entirely satisfactory.

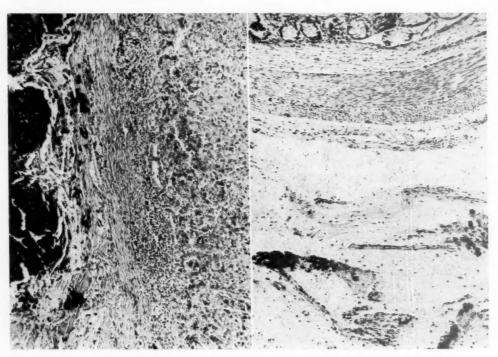


Fig. 1. Fig. 2.

Fig. 1.—Photomicrograph of liver showing thick fibrinous adhesions over the surface in which a large quantity of calcium can be seen.

Fig. 2.—Photomicrograph of cross section of intestine showing the fibrinous adhesions on peritoneal surface with intermingled flecks of calcium.

Autopsy Findings.—Externally, the infant appeared to be normal except for a markedly distended abdomen. The baby plus placenta weighed 11 pounds, 14 ounces. Since a considerable amount of the ascitic fluid had been lost during the process of delivery, no accurate measurement of the total amount could be obtained. On opening the abdominal cavity an estimated 1,000 c.c. of straw-colored fluid escaped. The intestines were found to be matted by greenish fibrinous adhesions into a small ball-like mass in the upper quadrants of the abdomen. The adhesions binding the bowel were easily fractured. Over the surface of the bowel, liver, and parietal peritoneum, small flecks of calcium could be grossly identified. The entire length of the gastrointestinal tract was carefully inspected and opened, but no area of perforation or obstruction could be identified. All the other organs of the body were entirely normal, both grossly and microscopically.

Pathological Diagnosis.—The diagnosis was meconium peritonitis, diffuse, marked, point of perforation not identified; and ascites, marked, due to above features.

#### Comment

The incidence of meconium peritonitis is uncommon. The occurrence of meconium peritonitis with ascites resulting in dystocia is even less common. The diagnosis of this condition before the second stage of labor is difficult and frequently will be missed even when x-rays are taken. These babies usually die during the second stage after the head has been delivered. If the diagnosis could be made before the second stage of labor, delivery by cesarean section would be the method of choice and probably a viable infant would be obtained; however, this infant would still face the hazard of laparotomy to release adhesions and close the perforation if it is still present.

## Summary

A case of meconium peritonitis with ascites resulting in dystocia is presented.

#### References

- Camp, R., and Roberts, M. H.: Am. J. Dis. Child. 78: 393, 1949.
   Franklin, A. W., and Hosford, J. P.: Brit. M. J. 2: 251, 1952.
- 3. Lattes, R.: Am. J. OBST. & GYNEC. 46: 149, 1943.

4635 WYANDOTTE

KANSAS CITY 12, Mo.

# PRELIMINARY REPORT OF AN ELECTROPLATING TEST OF URINE FOR PREGNANCY\*

Walter H. Hartung, Jr., M.D., and Herbert J. DeVauent, E.E., Toledo, Ohio

(From the Departments of Pathology and Bio-electrics, St. Charles Hospital)

ERTAIN physiological changes occur in pregnancy which are detectable by bioassay procedures, cervical mucus characteristics, vaginal smear cytology, skin tests, and chemical methods. At present, biological tests are universally used. In 1930, Aschheim<sup>1</sup> reported an accuracy of 98.6 per cent in detecting pregnancy by use of the mouse as a test animal. However, this method was costly and time-consuming. In 1931, Friedman, using the rabbit, reported 100 per cent accuracy in 92 cases. Of these, there were 47 clinically pregnant women, 25 of whom were in the last trimester of pregnancy and 22 in the first. Reinhart in 1933 reported 95.5 per cent to 96.6 per cent correct negative results and 97.4 per cent to 98.8 per cent correct positive results for the Friedman test in 865 cases. This procedure required 48 hours for completion. In 1948, Wiltberger and Miller,6 using the male frog, Rana pipiens, reported 100 per cent accuracy in the first trimester of pregnancy. Unless the urine sample was concentrated by some technique such as with chloroform, kaolin, or acetone, however, Reinhart, Caplan. and Shinowara<sup>5</sup> could obtain only 74 per cent accuracy with the frog. Davis and Ferrill<sup>2</sup> in 1932 reported 98.3 per cent accuracy when immature male or female rats were utilized. In their series there were 77 clinically proved pregnant women. Of these, 48 were 6 weeks to 3 months pregnant, while 29 were 4 to 10 months pregnant. Some observers, however, contest the accuracy of this test when reported in less than 24 hours.

Surveys of present methods for detecting pregnancy suggest that a rapid, economical, sensitive, and specific test for pregnancy without the use of animals is quite desirable. It is the aim of this paper to describe the method and report preliminary results of an electroplating test for pregnancy used on unconcentrated urine specimens of pregnant and nonpregnant women, adult men, and children in 1,500 routine hospital admissions (Group I) and on 150 women from the offices of specialists in obstetrics and gynecology (Group II).

#### Method

Ten milliliters of a freshly voided random urine sample or one that has not been refrigerated more than 12 hours is placed in a vial, brought to room temperature, adjusted to a pH of 4.0, and attached to the electroplating unit

<sup>\*</sup>This work was supported in part by a grant from the St. Charles Hospital Research Foundation.

(Fig. 1). This is composed of a copper cathode and silver anode spaced 1.0 cm. apart. A voltage of 12 volts (direct current) is then applied to the copper cathode, the current being 0.1-0.5 ampere. After 5.0 seconds of charge the vial is removed from the electroplating test unit and the anode examined macroscopically or by means of light reflected into, and measured by, a photoelectric cell. After 100 tests the silver anode should be replaced.

Macroscopic Examination of Anode.—As soon as the voltage is applied, gas formation is evident along the cathode. This varies in intensity with the specimen. At the end of the 5.0 seconds a fine granular bluish deposit has formed over the surface of the anode. Some of this deposit is superficial and may fall freely into the urine sample; the remainder of the superficial layer can be wiped off the anode easily with a cloth. Beneath this superficial deposit on the anode there is another deeper deposit which varies in color and removability. It may be dull silver or a very dull, granular black (Fig. 2). Between these extremes there are varying shades of intensity with occasional silver, gold, or black spots. In some cases these deeper, primary deposits can be wiped off partially with a cloth, while in most cases they can be removed only with the aid of some substance such as steel wool or dilute nitric acid. In some cases the anode will reveal a smooth, shiny black deposit.

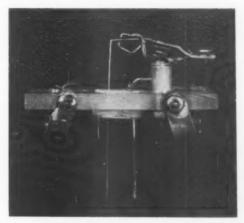


Fig. 1.—Close-up view of electrodes of plating unit.

Photoelectric Examination of Anode.—After wiping the superficial deposits from the anode with a cloth, the anode is placed into a photoelectric recording unit (Fig. 3). Within this unit two light sources impinge on the surface of the silver strip and the diffused light reflected from the coated surface activates a photoelectric cell which, in turn, supplies current to a milliammeter. The meter scale is calibrated to read from 0 to 5 Ma. while interpolations allow readings in tenths of a unit.

Interpretation of Test Result.—The corresponding macroscopic and photoelectric readings in our experiments have been interpreted as follows:

MACROSCOPIC APPEARANCE OF DEEP DEPOSITS	PHOTOELECTRIC CELL READING	INTERPRETATION
No deposit to sparse dull black	0-2.9	Negative
Sparse to medium dull black deposit	3.0-3.4	Doubtful; suggest repeat study
Medium to heavy dull black deposit	3.5-5.0	Positive

When a shiny black deposit is obtained this must be recognized by the observer and considered to be a doubtful reading regardless of the meter reading it develops.

#### Results

Clinical Tests.—All of the cases of both Groups I and II had complete clinical follow-ups. Included in the 1,500 patients of Group I were men,

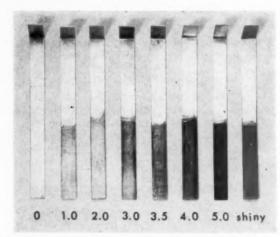


Fig. 2.—Photograph of anodal deposits. The shiny black deposit seen at the far right is interpreted as a doubtful result and should prompt a repeat study. The anode at the far left represents the silver strip before it is exposed to the voltage in the electroplating unit.

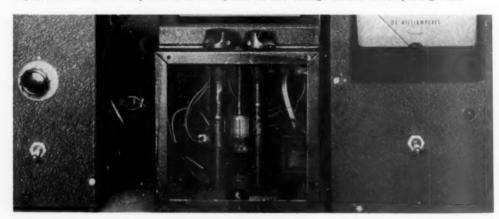


Fig. 3.-Close-up view of photoelectric recording unit.

women, and children of all ages and with varying kinds and severity of illnesses, representing routine admissions to St. Charles Hospital. Many of the pregnant women of this group had complications of pregnancy, such as threatened or complete abortion, and many were admitted for delivery. These types of cases were chosen deliberately to place the test method under the most adverse conditions possible. The earliest positive test result was obtained at 17 days, 3 at 19 days, and 6 at 21 days of pregnancy. The greatest accuracy, however, was obtained at approximately 6 weeks. On the average, the test result became negative within 72 hours after the cessation of the viable pregnancy. In one case, however, it remained positive until  $4\frac{1}{2}$  months post partum, at which time the mother stopped breast-feeding her child.

There were 1,080 women in Group I; of these, 301 were pregnant. The trimester of pregnancy and the results of testing the urine of these women are shown in Table I. Forty false-negative results were obtained. These are analyzed according to clinical findings and trimester of pregnancy in Table II. Eighteen doubtful results occurred in the 301 clinically pregnant women. These are analyzed according to the trimester of pregnancy and clinical findings in Table III.

TABLE I. ROUTINE HOSPITAL ADMISSIONS OF 301 CLINICALLY PREGNANT WOMEN (GROUP I)

PERIOD OF	ELEC	0/0		
GESTATION	POSITIVE	NEGATIVE	DOUBTFUL	ACCURACY
First trimester	105	11	9	84.0
Second trimester	15	6	3	62.5
Third trimester	123	23	6	82.0
Total	243	40	18	80.7

TABLE II. ANALYSIS OF 40 FALSE-NEGATIVES (GROUP I, FROM TABLE I)

First Trimester.—	
Threatened abortion	5
Uncomplicated pregnancy	5
Hyperemesis gravidarum	1
**	11
Second Trimester.—	
Abdominal cramps	. 3
Palpable pelvic mass	2
Vaginal discharge	1
	6
'hird Trimester.—	
Active labor	20
Threatened abortion (6 months)	1
Allergic dermatitis (7 months)	1
Repeat cesarean section (8 months)	1
	23

Table III. Analysis of 18 Doubtful Results Occurring in 301 Clinically Pregnant Women (Group I)

First Trimester.—	
No complications	5
Hyperemesis	1
Incomplete abortions	2
Threatened abortion	1
	9
Second Trimester.—	
No complications	3
Third Trimester.—	
Active labor	9

Table IV. Routine Hospital Admissions of 779 Clinically Nonpregnant Women (Group I)

AGE	ELECT	0/0		
(YEARS)	POSITIVE	NEGATIVE	DOUBTFUL	ACCURACY
Under 14	2	41	3	89.13
14-50	28	429	23	89.38
Over 50	4	241	8	95.25
Total	34	711	34	91.27

Table V. Analysis of 34 False-Positives Occurring in 779 Clinically Nonpregnant Women (Group I)

WOMEN (GROUP I)	
Under 14 years old.—	
Acute appendicitis	$\frac{1}{2}$
Bronchopneumonia	1
	2
14 to 50 years old.—	
Acute appendicitis	2
Acute cystitis	2
Acute colitis	1
Acute cholecystitis	1
Acute gastritis	1
Acute pelvic inflammatory disease	1
Chronic cervicitis	3
Chronic pelvic inflammatory disease	1
Chronic tonsillitis	1
Chronic duodenal ulcer	1 1 1
Fracture of bone	1
Hyperthyroidism	1 1 2 1 1 1 1 2 1 1
Premenopause	1
Delayed menstruation (7 days)	2
Adenocarcinoma of ovary	1 -
Functional uterine bleeding	1
Retroversion of uterus	1
Atopic eczema	1
Urinary tract stones	2
Cystic disease of breast	1
Peritoneal adhesions	1
Following electroshock therapy	1
	28
Over 50 years old	
Chronic cholecystitis	1
Hypertension	1
Fracture of bone	2
The state of the s	1 1 2 4

Table VI. Analysis of 34 Doubtful Results Occurring in 779 Clinically Nonpregnant Women (Group I)

	., (	
Unde	r 14 years old.—	
Ac	ute appendicitis	2
Chi	ronic tonsillitis	$\frac{2}{1}$
		3
14 to	50 years old.—	
An	xiety reaction	9
	pressive reaction	4
	acture of bone	3
	st of ovary	3
$\mathbf{U}_{\mathbf{p}}$	oper respiratory infection	2
Ac	ute appendicitis	1
Ch	ronic cervicitis	1
		23
Over	50 years old.—	
Ar	nxiety reaction	3
	pressive reaction	2
	neumonia	1
	reinoma	1
Ch	ronic cholecystitis	1
	•	8

Of the 1,080 women in Group I, 779 were nonpregnant. The ages of these women and the results of testing the urine are shown in Table IV. Thirty-four false-positive results were obtained. These are analyzed according to age and clinical findings in Table V. Thirty-four of the 779 nonpregnant women showed doubtful results. These are analyzed according to age and clinical findings in Table VI. In most cases repeat studies resolved the doubtful classifications.

Group II included 144 clinically known pregnant women without complications and 6 clinically known nonpregnant women. This type of material was chosen to place the test method under conditions similar to those under which it ordinarily would be used. Admittedly, this group is small. The results of the electroplating test among the 144 clinically pregnant women are shown in Table VII. It is notable that no errors occurred in the first trimester. Nine false-negative results were obtained, 2 in the second trimester and 7 in the third. None of these had any detectable complications at the time of the study. There were 5 doubtful test results in this group, constituting an approximate 3.5 per cent incidence. None of these had any complications; 2 were in the second and 3 in the third trimester. In this group, as in Group I, most doubtful results were resolved by repeat studies.

Table VII. Cases From Offices of Obstetrics and Gynecology Specialists (144 Clinically Pregnant Women, Group II)

PERIOD OF GESTATION	ELEC	%		
	POSITIVE	NEGATIVE	DOUBTFUL	ACCURACY
First trimester	29	0	0	100.0
Second trimester	51	2	2	94.4
Third trimester	50	7	3	83.3
Total	130	9	5	90.27

Of the 6 nonpregnant women, 3 were in the 14 to 50 year age group and yielded negative results, while 3 were over 50 years of age and postmenopausal and yielded false-positive results.

Table VIII. Results of Animal and Electroplating Tests on 44 Clinically Pregnant Women (First Trimester)

TEST	POSITIVE BESULTS	% ACCURACY	NEGATIVE RESULTS	CLINICAL FINDINGS IN NEGATIVE RESULTS			
				MONTHS PREGNANT	NO COMPLI- CATION	THREATENEI ABORTIONS	
Frog	19	43.2	25	1	4	2	
				3	5 -	7	
Rabbit	37	84.1	7	1	2	-	
				3	-	1	
Electroplating	40	91.0	4	1	-	=	
				2 3	-	2 2	

Comparison With Animal Tests.—In Group I, 70 of the 1,080 women studied had animal tests done along with the electroplating test. These are compared in Tables VIII and IX. Of these, 44 were pregnant clinically, yielding a 43.2 per cent accuracy with the frog test, 84.1 per cent with the rabbit test, and 91.0 per cent with the electroplating test. Of the 70 women, 26 were not pregnant clinically, yielding a 98.2 per cent accuracy with the frog and the rabbit tests and a 61.5 per cent accuracy with the electroplating test. These

results were obtained in pregnant women having a complicating disease state or disturbed pregnancy such as a threatened abortion. Eight of these women were one, or less than one, month pregnant. Admittedly, again, this comparative study with animal tests involves only a small number of eases. Further studies are being done.

TABLE IX. RESULTS OF ANIMAL AND ELECTROPLATING TESTS ON 26 CLINICALLY NONPREGNANT WOMEN

TEST	NEGATIVE RESULTS	% ACCURACY	POSITIVE RESULTS	CLINICAL FINDINGS IN POSITIVE RESULTS
Frog	25	96.2	1	Aborted 24 hours previously Renal calculus; hypermenorrhea 3—Functional uterine bleeding 1—Acute appendicitis; corpus luteur cyst of ovary 1—Ruptured corpus luteum cyst of ovar 1—Delayed menstruation 1—Hypermenorrhea; renal calculus 1—Four months post partum 1—Chronic cervicitis 1—Menopause
Rabbit	25	96.2	1	
Electroplating	16	61.5	10	

Chemical Analysis of Anodal Deposit.—Preliminary chemical analyses of the deposits on the anode have been done. The dull black deposit cannot be wiped from the anode; it is soluble in dilute nitric acid. After evaporating it to dryness in a carbon electrode, the deposited material was subjected to are spectrographic analysis. No metals other than copper and silver could be detected. Infra-red absorption analysis failed to produce a spectrum, indicating that the material is not organic in nature. When a portion of the anode with the black deposit was introduced into a combustion tube, however, a definite evolution of carbon dioxide and water was obtained. Careful reduction of a coated electrode in a stream of hydrogen produced a whitish deposit. This could have been due to reduced silver salts. Ignition in oxygen produced a typical tarnish resulting from copper oxide and arising from the copper content of the anode. Other studies revealed that the deposit contained a trace of chloride, no phosphorus, a minute amount of nitrogen, and sulfur.

#### Comment

In these preliminary studies the electroplating test has yielded an 84 per cent accuracy in 125 women in the first trimester of pregnancy in spite of complicating disease states. When used to detect uncomplicated pregnancy in the first trimester, a 100 per cent accuracy was obtained. Further studies are being conducted with these groups. In our experience the doubtful results have presented no major problem since most of these can be resolved by repeat studies in a few hours or days. In an obviously pregnant woman or in one proved to be pregnant by a test animal, however, a doubtful reading (3.0 to 3.4) may represent pregnancy earlier than 6 weeks or a disturbed pregnancy. In several such cases in our series the woman was threatening to abort or aborted within 24 to 48 hours. This suggests that the electroplating test may be of value not only in detecting pregnancy, but also in following the course of gestation after the diagnosis has been established.

# Summary

A preliminary report of an electroplating test for the detection of pregnancy is described. The test is done on a 10 ml. aliquot of a freshly voided

random sample of urine, which is brought to room temperature, adjusted to a pH of 4.0, and charged for 5 seconds with 12 volts direct current electricity applied through silver and copper electrodes. The urine of pregnant women causes a black substance to be deposited on the anode.

Two groups of patients were studied. Group I consisted of 1,500 routine hospital admissions including pregnant and nonpregnant women, adult men, and children. Group II consisted of 150 patients from offices of specialists in obstetrics and gynecology. All cases had complete clinical follow-ups. Among 125 women in the first trimester of pregnancy, including those with complications of pregnancy (Group I), 84.0 per cent accuracy was found. Among 29 clinically known pregnant women without complications, an accuracy of 100 per cent was found.

Parallel tests of frog, rabbit, and electroplating were carried out in 70 cases. The electroplating test yielded a 91 per cent accuracy in 44 clinically pregnant women and a 61.5 per cent accuracy in 26 clinically nonpregnant women. Of these 70 women, some were less than one month pregnant, others had a disturbed pregnancy such as threatened abortion, and others had a disease state complicating the pregnancy.

Preliminary studies indicate that complications of pregnancy, such as threatened abortion, are accompanied by changes in the electroplating test, suggesting that it may be a valuable tool not only for detecting pregnancy but also for following the course of gestation.

# References

- Aschheim, S.: AM. J. OBST. & GYNEC. 19: 335, 1930.
   Davis, M. E., and Ferrill, H. W.: AM. J. OBST. & GYNEC. 23: 567, 1932.
   Friedman, M. H., and Lapham, M. E.: AM. J. OBST. & GYNEC. 21: 405, 1931.
- 4. Reinhart, H. L.: Am. J. Clin. Path. 3: 9, 1933.
- 4. Reinhart, H. L.; Am. J. Clin. Fath. 5. 2, 1005.
  5. Reinhart, H. L., Caplan, L. J., and Shinowara, G. Y.: Am. J. Clin. Path. 21: 624, 1951.
- 6. Wiltberger, P. B., and Miller, D. F.: Science 107: 198, 1948.



# Gynecology

#### OVARIAN HILUS CELLS

JAMES A. MERRILL, M.D., \* SAN FRANCISCO, CALIF.

(From the Department of Obstetrics and Gynecology, University of California School of Medicine)

WHILE the main source of androgen in the female is the adrenal cortex, androgens are probably produced by the ovary. In an attempt to localize the ovarian source of androgens, attention has been given to epitheloid cells commonly found in the hilus of the adult ovary. These cells, most thoroughly investigated by Berger,<sup>2, 3</sup> bear a morphologic and perhaps a functional similarity to the testicular interstitial cells of Leydig. Indeed, Brannan,<sup>6</sup> whose studies were the first to appear in English literature, described them in the hilus and tunica of the testis as well as the ovary. Sternberg<sup>35</sup> recalled attention to these earlier works, coined the term "hilus cells," and stimulated interest in their possible androgenic function.

Hilus cells should be considered a normal finding,  $^{9, 35}$  for it is probable, with careful examination, that such cells may be found invariably in the ovaries of adult women. They vary in shape from elongate and fibrilloid to the more usual polygonal or oval forms and range in size from 15 to 25  $\mu$  in diameter. The distinct nuclei are large, spherical, and vesicular, containing one or more prominent nucleoli (Fig. 1). Female sex chromatin patterns in the nuclei of hilus cells have been described. The cytoplasm is abundant, acidophilic, and frequently vacuolated, and contains variable amounts of stainable lipid. A golden-brown pigment, presumably lipochrome,  $^{35}$  is a characteristic, though not constant, finding.

Rarely, the cytoplasm contains rodlike, doubly refractile, acidophilic inclusions—the so-called crystalloids of Reinke (Fig. 2). Such inclusions, probably protein in nature, the function and/or significance of which is unknown, are a specific, albeit uncommon, finding in testicular Leydig cells. Their presence may identify Leydig cells or hilus cells, but their absence does not preclude identification. The use of Bouin or Zenker fixative and strong acid stains increases the frequency with which these inclusions are found.

The most characteristic identifying feature of these cells is their location in the hilus of the ovary. Found in nests or clusters, they are more numerous

<sup>\*</sup>Markle Scholar in Medical Science.

of

e

ls

y

y

d to n

e, ie io n g n

of a

S,

S.

n

near the poles of the ovary but are seen also in the cortex. They are found in close relationship to nerve (Figs. 1 and 3); hence, the earlier suggestion that they arose from the chromaffin system, or were sympathicotropic.<sup>2, 35</sup> They also bear close relationship to blood vessels and lymphatics (Fig. 3), from which they may be separated only by endothelium. The nests of hilus cells are frequently found to be well supplied with small blood vessels.

Luteinized theca cells (Fig. 4) resemble hilus cells, especially those present in the cortex, even to the presence of granular cytoplasm with brown pigment. Measurements reveal their size to be in the same range as hilus cells. The only positive differentiating feature is the presence of crystalloids in hilus cells. Additional similarity of hilus and theca cells is apparent when it is realized that the embryologic formation of ovarian theca cells and testicular Leydig cells is homologous; both arise from undifferentiated mesenchyme in the presence of granulosa cells and Sertoli cells, respectively<sup>11, 19, 22, 29</sup> (Figs. 5 and 6).

There is also a morphologic similarity between hilus cells and adrenal cortical cells. The organoid arrangement and encapsulation of the latter usually serves to distinguish them (Fig. 8).

The origin of hilus cells is in question. Histochemical evidence does not confirm their relationship with the chromaffin system or their origin from non-myelinated nerve, per se. 6, 35 A more reasonable concept is that they arise from either undifferentiated mesenchyme, as is the case in the testis, or from fibroblasts. 16, 24 Nerve may well serve as an organizer. They are said to be present at birth. 35 However, in a personal review of the ovaries from 70 female infants, 16 of whom were newborn and 40 of whom were under one year of age, no hilus cells were identified, although frequent remnants of the mesonephros were found and frequent hyperplasia of luteinized theca about atresic follicles was noted (Fig. 7). Adrenal rests were identified in the ovarian hilus or broad ligament in 2 of these 70 infants (Fig. 8).

TABLE I. OVARIAN HILUS CELL TUMORS

AUTHOR	AGE OF PATIENT	SIZE OF TUMOR	REINKE CRYSTAL- LOIDS	17-KETO- STEROIDS	IMPROVE- MENT	COMMENTS
Berger <sup>3</sup>	50	0.5 cm.	Absent	-	Yes	Normal menses
Sternberg35	86	1.2 cm.	+	Normal		Hypertension
Sternberg35	64	1.0 cm.	+	Normal	Yes	V
Waugh41	46	4 cm.	+	Slightly ele- vated	Yes	17-ketosteroids returned to normal
Sachs <sup>28</sup>	47	1.8 cm.	+	Normal	_	In addition ectopic adrenal rest
Langley <sup>18</sup>	18	6 cm.	Absent	Upper normal	Yes	17-ketosteroids returned to normal
Young42	27	9 cm.	Absent		Yes	Pregnant
Pedersen <sup>26</sup>	65	"Small"	Absent	Elevated	Partial	Hypertension, diabetes
Berkheiser4	50	2.0 cm.	Absent		Yes	Hypertension
Merrill	54	2.3 cm.	Absent	Upper normal	Yes	Hypertension, diabetes

Assumptions<sup>3, 4, 6, 12, 14, 18, 26, 28, 35, 36, 37, 39, 40, 41</sup> regarding possible function of hilus cells stem from their similarity to Leydig cells, their relative exclusive occurrence in *mature* ovaries, and clinicopathologic observations. Brannan<sup>6</sup> implied a hormonal activity because he observed hyperplasia and hypertrophy of these cells during pregnancy. Similar observations during pregnancy and following administration of chorionic gonadotrophin have been reported by Sternberg,<sup>36</sup> who also noted an increase in urinary excretion of 17-ketosteroids following gonadotrophin. He suggested that this was related to increased

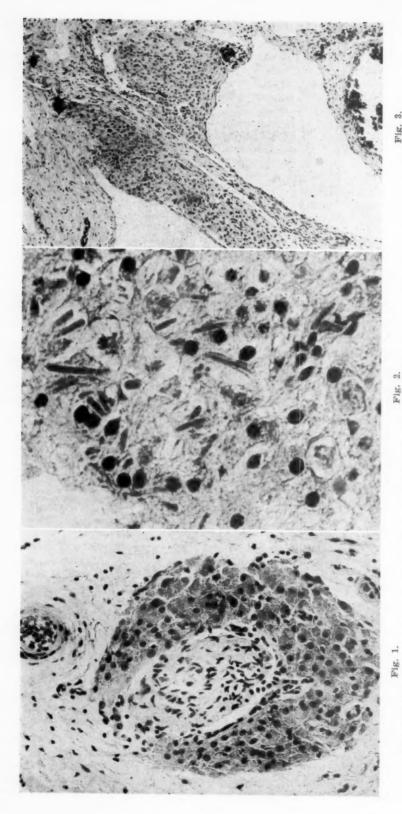


Fig. 1.—Ovarian hilus cells closely associated with nerve from a normal adult woman. The cells are polygonal with abundant, granular, vacuolated cytoplasm and distinct vesicular nuclei containing one or more nucleoli.

Fig. 2.—Ovarian hilus cells with abundant crystalloids of Reinke from a normal adult woman. Fig. 3.—Ovarian hilus cells from a normal adult woman. Note close relationship to vessels, lymphatics, and small nerve.

androgen production by hilus cells. Luteinized theca, particularly about atresic follicles, responds to pregnancy with similar hypertrophy, hyperplasia, and increased activity.

Specific examples of the presumed function of hilus cells have been reported. 12, 14, 30 Three years ago, Gordan and associates 12 reported from our institution 2 cases of ovarian agenesis with androgenic manifestations and coined the term, now commonly used, of "gonadal dysgenesis." The gonadal anlage in each case contained epitheloid cells, identified as hilus cells and presumed to be responsible for the clinical masculinization. Both of these patients had the sex chromatin pattern of a male. The relationship between hilus cells, in such gonadal anlage, and masculinizing features is not constant, however, for these cells have been observed in similar patients without masculinizing features. 14, 15 Moreover, the majority of such patients are genetic males. 15

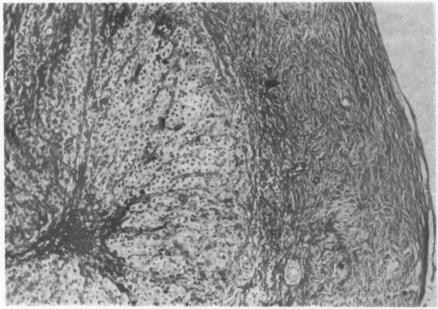


Fig. 4.—Hyperplasia of luteinized theca cells in the ovarian cortex of an adult non-pregnant woman. The reticular connective tissue separating cords of cells around the atresic follicle is apparent.

A personal review of the gonads of 4 additional cases of gonadal dysgenesis revealed similar cell nests in 2 cases. Neither of these patients showed masculinizing features. One of these patients had a female sex chromatin pattern; the other, male. In each of the 4 cases in which hilus cells were identified, the patient was 14 years of age or older. In the 2 cases in which hilus cells were not identified, the patients were 4 and  $6\frac{1}{2}$  years of age, respectively. This is similar to the age frequency of their identification in normal ovaries.

Another specific functional activity has been suggested by Shaw and Dustur,<sup>30</sup> who noted hilus cells in the ovaries of patients with carcinoma of the uterus and concluded that these cells were possibly carcinogenic. Husslein<sup>15</sup> likewise proposed etiological significance to these cells in cases of endometrial hyperplasia. Such observations and claims, however, must be disregarded if we accept the presence of hilus cells as a constant finding in adult ovaries.<sup>13</sup> Similar observations and associations have been made for thecomatosis, which may resemble hyperplasia of hilus cells, and cortical stromal hyperplasia, but with sounder evidence.<sup>5</sup>

The most significant evidence that hilus cells are a source of androgen is the observation of masculinization associated with hyperplasia or tumor. Hyperplasia of hilus cells has been noted in patients with varying degrees of masculinization.<sup>8, 25, 35, 37</sup> However, the cause-and-effect relationship is not



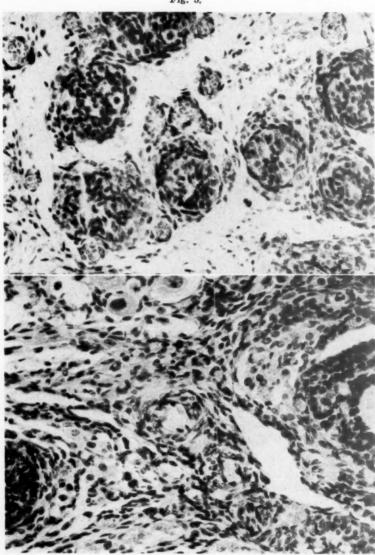


Fig. 6.

Fig. 5.—Fetal testis. Note Leydig cells around the developing tubules.

Fig. 6.—Fetal ovary. Note the theca cells around the granulosa cells of the developing follicles. (Compare with Fig. 5.)

absolutely clear. We have observed significant hyperplasia of hilus cells in one case; this was an incidental finding (Fig. 9). This patient had no evidence of excess androgen stimulation.

Berger<sup>3</sup> was the first to report a case of a tumor presumed to be of hilus cell origin. Since then additional cases have been reported as indicated in

n

r.

of ot Table I. Characteristically, these tumors have been benign, and were found in menopausal or postmenopausal women with gross masculine features. Excretion of 17-ketosteroids has been normal or slightly elevated. The tumors have been small, usually not enlarging the ovary. The record of normal pelvic

Fig. 7.

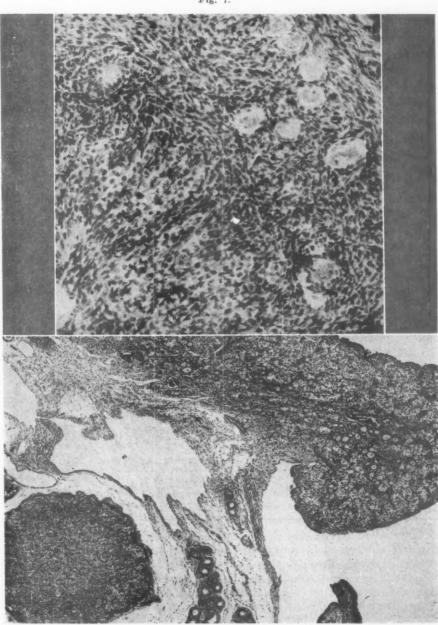


Fig. 8.

Fig. 7.—Newborn ovary. Note hyperplastic luteinized theca about follicle. This is a frequent finding in infant ovaries.

Fig. 8.—Newborn ovary with adrenal cortical rest in the mesovarian. Note the characteristic organoid pattern and encapsulation.

examination is common. Features characteristic of Cushing's syndrome have been observed. Removal of the tumor has produced some regression in the degree of masculinization.

A case recently treated at the University of California Medical Center is presented as a possible example of such a tumor.

Case 1.—U. C. H. No. 254901, a 54-year-old mother of 2 children, was followed at the University of California Medical Center with complaints of obesity, increased hair growth, weakness, and boils. Her menses stopped spontaneously at the age of 35, when she first noted increased hair growth on her face, arms and body. The hirsutism eventually required shaving every day. She gained weight and became increasingly muscular. During the 5 years preceding admission she noted deepening of her voice.

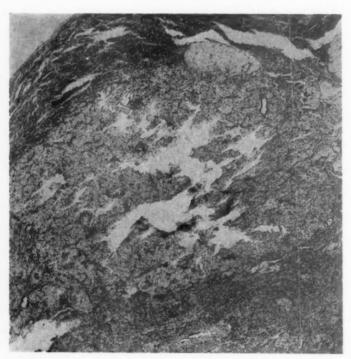


Fig. 9.—Hilus cell hyperplasia in the ovary of a postmenopausal patient. The patient showed no evidence of excessive androgen stimulation.

The extreme masculine appearance of the patient is well seen in Fig. 10. Abdominal striae were present. Pelvic examination revealed a female escutcheon with slight clitoridal enlargement but was otherwise normal.

Observations of hypertension, polycythemia, and diabetes mellitus were made on numerous occasions, although the hypertension disappeared following an acute myocardial infarction.

Adrenal function studies were interpreted as showing normal baseline function and capacity. Urinary 17-ketosteroid and 17-hydroxycorticoid excretion was normal (14.4 mg, per 24 hours and 10.0 mg, per 24 hours, respectively). Plasma hydrocortisone was also normal (16.7  $\mu$ g per cent). Stimulation with 20 units of intravenous ACTH (8 hours) produced the expected rise in 17-ketosteroid and 17-hydroxycorticoid excretion (32 mg, per 24 hours and 60.4 mg, per 24 hours). Plasma hydrocortisone rose to 34  $\mu$ g per cent. FSH was positive at 5 and negative at 80 mouse units. Retroperitoneal pneumograms revealed no abnormalities.

Ve

he

18

at

air

en

lly ng

al

al

11-

id

g.

(6

18

Because of normal adrenal studies, and after 2 years of observation and study, pelvic exploration was done. This revealed surgically absent left adnexa and right oviduct. The remaining right ovary was normal in size, but was nearly replaced by a 2 cm. soft, brown tumor. The gross appearance is seen in Fig. 11. Microscopically (Figs. 12 and 13), a thin margin of ovarian cortical stroma surrounded the medullary tumor which was nonencapsulated and which was composed of large masses of cells arranged in sheets and nests. The cells, as seen in the photomicrographs, were uniform and polyhedral with round, distinct nuclei. The cytoplasm was eosinophilic with slight vacuolation. Many cells contained abundant brown pigment. Fat stain revealed finely dispersed fat droplets in many cells. Crystalloids of Reinke were not identified.

Adrenal function studies, postoperatively, revealed identical 17-hydroxycorticoid levels, but 17-ketosteroid levels were approximately 9 mg. per 24 hours less than preoperatively (5.2 mg. per 24 hours). ACTH stimulation and hydrocortisone suppression were again



Fig. 10.-Photograph of the patient, Case 1, with ovarian hilus cell tumor.

normal. The values were the same as the preoperative ones if the 9 mg. difference in 17-ketosteroid level was subtracted (17-ketosteroids—stimulation: 15.6 mg. per 24 hours, suppression: 3.0 mg. per 24 hours; 17-hydroxycorticoids—stimulation: 61.4 mg. per 24 hours, suppression: 4.8 mg. per 24 hours). These data indicate an extra-adrenal source of androgen, presumably the ovarian tumor, which did not respond as adrenal tissue. The details of adrenal function studies will be presented at greater length in a separate report. Since operation, there has been slight but definite regression of masculinizing features.

This tumor, while morphologically similar to previously reported hilus cell tumors, did not contain Reinke crystalloids. Moreover, in 5 of 9 previously reported hilus cell tumors, such crystalloids were not found; nor is this surprising, since crystalloids are found in as few as 6 per cent of testicular Leydig cells.<sup>24</sup> In the absence of crystalloids, it may be difficult to say whether such a tumor is of luteinized theca, adrenal cortical, or hilus cell origin.

Adrenal cortical cells are morphologically similar to hilus cells. Adrenal rests are known to occur in the ovarian hilus (Fig. 8) and, as previously noted, were found more readily in infant ovaries than were hilus cells. It has been stated<sup>4, 35</sup> that there should be little difficulty in distinguishing adrenal rests

from hilus cell nests because the former are sharply circumscribed, encapsulated, and show an organoid structure with cell cords centripetally arranged, duplicating the normal adrenal cortex. However, in the case of tumors arising from adrenal cortical rests, the distinction may not be easy. This is demonstrated by the following case:

CASE 2.—U. C. H. No. 223095, a 49-year-old nurse, complained of 2 years of increased facial and body hair, receding hairline, spotty alopecia, a 10-pound weight loss, and increasing hoarseness. Menses ceased spontaneously at the age of 31, several months following a pelvic adnexal operation.

The patient's general appearance was definitely masculinized and she shaved irregularly. The scalp hair was thin. The clitoris was slightly enlarged. The remainder of the pelvic examination was normal.

Routine laboratory data were normal.

Urinary 17-ketosteroid excretion was elevated (19.8 and 22.2 mg. per 24 hours), rose briskly (48.9 mg. per 24 hours) with ACTH stimulation, and was not suppressed with intravenous hydrocortisone. The 17-hydroxycorticoid excretion was normal (7.4 mg. per 24

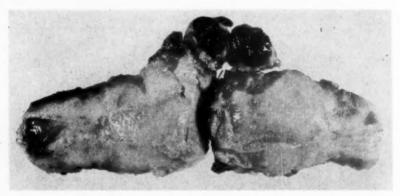


Fig. 11.—Case 1. Ovarian hilus cell tumor. Uterus and ovary opened. Ovary replaced by a soft brown tumor. A thin shell of ovarian tissue is seen.

hours and 8.4 mg. per 24 hours) and responded to ACTH stimulation by a rise to 44 mg. per 24 hours, but was suppressed to only 29 mg. per 24 hours with intravenous hydrocortisone. Retroperitoneal pneumograms did not demonstrate any evidence of adrenal tumor.

Since adrenal function studies indicated excessive adrenal androgen production, both adrenal glands were explored. No evidence of tumor or hyperplasia was found. Instead, biopsies revealed hypoplasia of both glands. In search of accessory adrenal tissue, pelvic exploration was carried out. The right adnexa were absent. The left ovary was normal size but was nearly replaced by a solid 2.8 cm. elive-brown tumor.

The histology of this tumor is seen in Fig. 14. It is composed of sheets of rather uniform, large epithelioid cells with prominent cytoplasm, containing brown pigment granules and small vacuoles. The tumor was not encapsulated. Strands of cells blend into the adjacent ovarian cortical stroma. The cells do not have an organoid formation. The nuclei are round with prominent chromatin network and one or 2 nucleoli. Primarily because of the adrenal function studies, a diagnosis of adrenal cortical rest tumor was made.

Postoperatively, the 17-ketosteroid exerction and activity became normal and remained so for at least one year. There was slight, but definite, decrease in the masculine appearance of the patient.

Grossly and microscopically, the tumors from these 2 cases are similar, and maybe they are the same type of tumor. However, in the first case, the adrenal function was determined to be normal prior to and following removal of the tumor, and thus the androgenically active tumor was not of adrenal origin. In the second case, studies indicated excessive adrenal androgenicity,

which disappeared following removal of the ovarian tumor, suggesting the adrenal nature of this neoplasm. Thus, metabolic function, rather than morphology, may indicate the exact nature of such lipoid tumors.

Fig. 12.

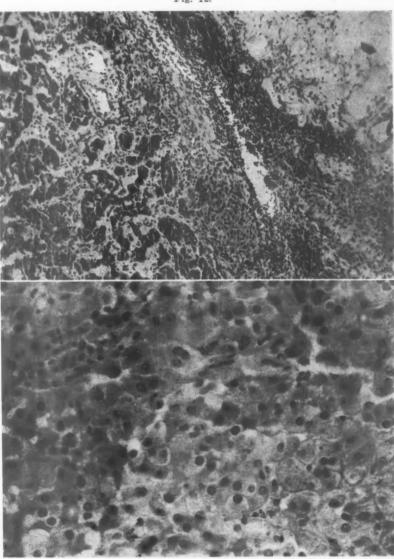


Fig. 13.

Fig. 12.—Case 1. Ovarian hilus cell tumor. Section from the edge of the tumor demonstrates the lack of encapsulation and the nests of cells comprising the tumor.

Fig. 13.—Case 1. Ovarian hilus cell tumor. Sheets of cells with granular cytoplasm and lipochrome pigment. Round nuclei with prominent nucleoli are seen.

The similarity between hilus cells and luteinized theca has already been noted. Thus difficulty may arise in morphologically distinguishing Leydig cells or hilus cell tumors from extreme hyperplasia or tumor formation of luteinized theca cells, and, functionally, the distinction may be more difficult (Figs. 4 and 7). Numerous observations of masculinization associated with

thecal proliferation and luteinization have been made<sup>10, 27, 31-33</sup> and suggest androgenic as well as estrogenic properties of theca cells. The specific nature of the androgen produced by theca cells<sup>20, 21</sup> is open to speculation and may be related to progesterone or a conversion or by-product of the intermediate

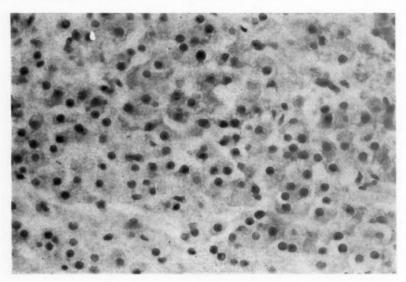


Fig. 14.—Case 2. Ovarian adrenal cortical rest tumor. The vacuolated cytoplasm, pigment granules, and suggestive cordlike arrangement are seen. Prominent nuclei and nucleoli are apparent.

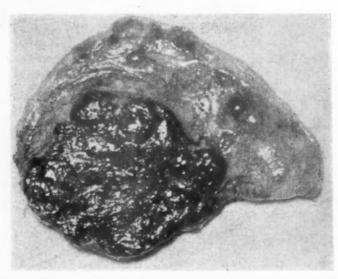


Fig. 15.—Case 3. Luteinized thecoma. Gross appearance of the ovary containing the yellow-brown tumor. The ovary measured 4 cm. in greatest dimension.

metabolism of this hormone. For example, a common feature of the Stein-Leventhal ovary is hyperplasia of luteinized theca, particularly about atresic follicles. Only recently Allen¹ suggested that the therapeutic effectiveness of wedge resection of the ovary results from removal of this excess theca in the medulla. Have these cells been mistaken for hyperplastic hilus cells? I am sure that they frequently are.

When a true thecoma becomes diffusely luteinized, it may be associated with some degree of masculinization and may appear morphologically similar to the tumors we have discussed. This is demonstrated with a case of a luteinized thecoma.

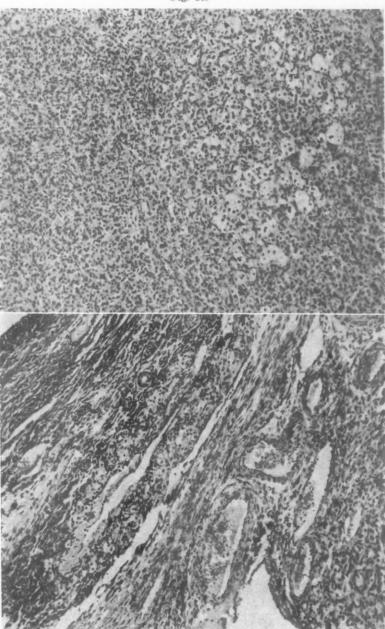


Fig. 17.

Fig. 16.—Case 3. Luteinized thecoma. The majority of the cells are large with a granular vacuolated eosinophilic cytoplasm containing occasional lipochrome pigment.

Fig. 17.—Case 3. Luteinized thecoma. A section from the edge of the tumor, including ovarian cortex. Note the luteinized theca cells surrounding the atresic follicle and compare them with the cells comprising the tumor.

CASE 3.—P. A. H. No. K·3471 was a 20-year-old Japanese girl who complained of amenorrhea and obesity. For 1½ years she had noted hoarseness, acne, and increased body hair. She had been amenorrheic for 7 months prior to the time of operation. Urinary 17-ketosteroids were reported as 15 mg. per 24 hours. X-ray examinations of the adrenal area and sella turcica were reported as negative. Blood chemistries, hemogram, and glucose tolerance tests were all normal.

Examination revealed a moderately obese, hirsute Japanese girl with generalized acne, especially over the back. There was no striae. Hair distribution was coarse. The escutcheon was female. The clitoris was not enlarged, and the pelvic examination revealed a right adnexal mass, estimated to be 4 to 8 cm. in greatest dimension.

At exploratory laparotomy the right ovary was found enlarged, with a thick white capsule and superficial cysts. It was removed and found to contain a 3 cm. yellow, solid tumor in the hilus (Fig. 15).

Microscopically, the tumor was nonencapsulated. In some areas it had the typical fibromatous appearance of a thecoma. For the most part, however, the cells were large and polyhedral and abundant acidophilic cytoplasm and occasional brown pigment (Fig. 16). Fat stains revealed finely dispersed fat droplets. Identification of these cells as luteinized theea was further facilitated by the finding of similar cells surrounding atresic follicles (Fig. 17).

#### Comment

Thus, while it may be possible to identify hilus cells with some certainty as they occur normally in the ovary, difficulty may arise in diagnosing a tumor arising from these cells. Moreover, the question as to whether an ovarian Leydig cell tumor represents neoplasia of pre-existing hilus cells or merely a masculinizing mesenchymoma (arrhenoblastoma or androblastoma) with predominance of Leydig cells cannot be answered. 18, 19, 25, 38, 40

Hilus cell tumors are very rare and occur in menopausal or postmenopausal women. Masculinizing mesenchymomas are seen more frequently and over a greater age span. Teilum<sup>40</sup> has grouped together many of the masculinizing and feminizing ovarian tumors under the classification of "androblastoma" arising from undifferentiated male-directed ovarian mesenchyme. MacKinlay<sup>19</sup> likewise includes a vast majority of masculinizing and feminizing tumors, including hilus cell tumors, under one classification. But he prefers to call them granulosa cell tumor, for, in his opinion, these cells are initially female-directed. They both agree, however, that ovarian mesenchyme has the ability to differentiate into granulosa, theca, Sertoli, or Leydig cells<sup>23</sup> and thus to produce a variety of tumors which may be functionally and morphologically similar.<sup>5</sup>

#### Conclusion

Ovarian hilus cells are clearly a specific morphologic entity, albeit of uncertain origin, and may be readily identified in sections of adult ovary, which include the hilus and broad ligament. The evidence for any specific function of these cells, in particular androgenic function, under normal or congenitally abnormal situations is not completely satisfactory. Hyperplasia of hilus cells has been observed in patients with androgenic manifestations, but has also been an incidental finding in the ovaries of women without evidence of excess androgen production. Ovarian tumors, composed of cells with morphologic characteristics of Leydig cells, do occur and are associated with masculinization. Such tumors may arise from hilus cells or from undifferentiated

1

d

1

1 ľ

9

n

a

e T

a

11 1

1d mesenchyme. The clinicopathologic features and age distributions of these tumors differ somewhat from other masculinizing ovarian lesions. usually precludes accurate diagnosis without pelvic exploration and ovarian sectioning. Moreover, the morphologic and functional similarity between hilus cells, adrenal cortical cells, and luteinized theca cells may offer difficulty in specific identification of such tumors.

While Leydig or hilus cell tumors are probably less rare than heretofore thought, they will explain very few cases of masculinization. Information relative to specific androgen production by the ovary is needed.

I wish to thank Dr. Felix Kolb for permission to use Case 2 and Drs. Johan V. Hultin and George Baba for permission to use Case 3.

### References

- Allen, W. N., and Woolf, R. B.: Am. J. Obst. & Gynec. 77: 826, 1959.
   Berger, L.: Compt. rend. Acad. d. sc. URSS 175: 907, 1922.
   Berger, L.: Rev. canad. de biol. 1: 539, 1942.

- 4. Berkheiser, S. W.: AM. J. OBST. & GYNEC. 73: 429, 1957. 5. Bigelow, Bradley: Obst. & Gynec. 11: 487, 1958.
- 6. Brannan, D.: Am. J. Path. 3: 343, 1927.
- 7. Davis, M. E., and Plotz, E. J.: Am. J. Obst. & Gynec. 8. Dougherty, C. M., Thompson, W. B., and McCall, M. C.: AM. J. OBST. & GYNEC. 76: 939, 1958. B., and McCall, M. C.: AM. J. OBST. & GYNEC. 76: 653, 1958.

- 9. Gardner, G. H., Greene, R. R., and Peckham, B.: Am. J. Obst. & Gynec. 73: 536, 1957.

  10. Geist, S. H., and Gaines, J. A.: Am. J. Obst. & Gynec. 43: 975, 1942.

  11. Gillman, J.: Contrib. Embryol. 210: 81, 1948.

  12. Gordan, G. S., Overstreet, E. W., Traut, H. F., and Winch, G. A.: J. Clin. Endocrinol. 15: 1, 1955.

  13. Greene, R. R., and Peckham, B. M.: Am. J. Obst. & Gynec. 61: 657, 1951.

  14. Greenblatt, R. B., Carmona, N., and Higdon, L.: J. Clin. Endocrinol. 16: 235, 1956.

  15. Grumbach, M. M., Van Wyk, J. J., and Wilkins, L.: J. Clin. Endocrinol. 15: 1161, 1955.

  16. Hooker, C. W.: Am. J. Anat. 74: 1, 1944.

  17. Husslein, H.: Ztschr. Geburtsh, u. Gynäk. 130: 32, 1948.

  18. Langley, F. A.: J. Clin. Path. 7: 10, 1954.

- Langley, F. A.: J. Clin. Path. 7: 10, 1954.
   MacKinlay, C. J.: J. Obst. & Gynaec. Brit. Emp. 64: 512, 1957.

- McKay, D. G., Hertig, A. T., and Hickey, W. F.: Obst. & Gynec. 1: 125, 1953.
   McKay, D. G., Robinson, D., and Hertig, A. T.: Am. J. Obst. & Gynec. 58: 625, 1949.
   Marchetti, A. A.: Am. J. Obst. & Gynec. 63: 294, 1952.
   Mossman, H. W.: In Engle, E. T., editor: Studies on Testis and Ovary: Eggs and Sperm, Springfield Ill., 1952, Charles C Thomas, Publisher, p. 196.
- Nelson, A. A.: Am. J. Path. 14: 831, 1938.
   Nokes, J. M., and Claiborne, H. A.: Ann. Surg. 143: 729, 1956.

- Nelson, A. A.: Ann. J. Path. 14. 831, 1936.
   Nokes, J. M., and Claiborne, H. A.: Ann. Surg. 143: 729, 1956.
   Pedersen, J., and Hamburger, C.: Acta endocrinol. 13: 109, 1953.
   Rottino, A., and McGrath, J. F.: Am. J. Obst. & Gynec. 45: 863, 1943.
   Sachs, B. A., and Spiro, D.: J. Clin. Endocrinol. 11: 878, 1951.
   Schiller, W.: In Meigs, Joe V., and Sturgis, Somers H., editors: Progress in Gynecology, New York, 1946, Grune & Stratton, Inc., p. 1.
   Shaw, W., and Dustur, B.: Brit. M. J. 2: 113,1949.
   Shippel S.: J. Obst. & Gynace, Brit. Emp. 57: 362, 1950.

- 30. Snaw, W., and Dustur, B.: Brit. M. J. 2: 113,1949.
  31. Shippel, S.: J. Obst. & Gynaec. Brit. Emp. 57: 362, 1950.
  32. Shippel, S.: J. Obst. & Gynaec. Brit. Emp. 57: 557, 1950.
  33. Shippel, S.: J. Obst. & Gynaec. Brit. Emp. 62: 321, 1955.
  34. Sohval, A. R., and Gaines, J. A.: Cancer 8: 896, 1955.
  35. Sternberg, W. H.: Am. J. Path. 25: 493, 1949.
  36. Sternberg, W. H.; Segaloff, A., and Gaskill, C. J.: J. Clin. Endocrinol. 13: 139, 1953.
- 37. Taliaferro, I., Wells, E. J., Kay, S., and Hoge, R. H.: A. M. A. Arch. Int. Med. 91: 675, 1953.
- Teilum, G.: Acta path. et microbiol. scandinav. 23: 252, 1946.
   Teilum, G.: In Meigs, Joe V., and Sturgis, Somers H., editors: Progress in Gynecology, New York, 1950, Grune & Stratton, Inc., Vol. II, p. 38.
- 40. Teilum, G.: Cancer 11: 769, 1958.
  41. Waugh, D., Venning, E. H., and McEachern, D.: J. Clin. Endocrinol. 9: 486, 1949.
  42. Young, W. R.: Illinois M. J. 100: 263, 1951.

# THE FATE OF THE CORPUS ALBICANS: A QUANTITATIVE APPROACH\*

ROBERT V. JOEL, M.D.,\*\* AND ALVAN G. FORAKER, M.D., JACKSONVILLE, FLA.

(From the Research Laboratory, Baptist Memorial Hospital)

DURING routine microscopic examinations of ovarian sections, the following observation became apparent: Ovaries from postmenopausal women seemed to have about the same number and prominence of corpora albicantia as those from premenopausal women.<sup>5</sup>

The ovary of a 26-year-old patient might contain 4 or 5 corpora albicantia. Frequently the ovary of a 61-year-old patient might present an essentially similar appearance with respect to the corpora albicantia. To the best of our knowledge, for each ovulatory cycle a corpus albicans should be formed.<sup>2</sup> We would then imagine that, after years of corpus albicans formation, the ovary of a 45-year-old woman would be packed with many of these structures. However, this is not true. One is hard pressed to demonstrate microscopically more than a dozen of the corpora albicantia in ovaries of women who have been ovulating for 25 years. Hertig³ states that corpora albicantia are found in postmenopausal ovaries and "even as menopause is reached, there are no abrupt changes in the pre- as compared to the early post-menopausal organs." Schneider and Bechtel¹ list frequency of ovulation as one factor contributing to the number of corpora albicantia in the senile ovary.

There are at least two possibilities concerning the apparent disappearance of many corpora albicantia over the productive life span of the average woman: (a) each corpus luteum does not form a corpus albicans; (b) the corpus albicans undergoes a form of resorption. The first statement seems implausible. Available literature contains no reference to the disappearance of corpora lutea without corpora albicantia formation. Ham² lists no alternative for the transition of the corpus luteum to the corpus albicans. We have never seen evidence of regression of a corpus luteum without hyalinization and fibrosis tending toward corpus albicans formation. The phenomenon of corpus albicans resorption most likely halts at or near menopause. As menopause is reached, the last few corpora albicantia formed apparently remain.

III.

mea

The initial study of the fate of the corpora albicantia was a planimetric evaluation of various components of the ovaries of pre- and postmenopausal women.

<sup>\*</sup>The investigation was supported by research grants from the National Cancer Institute. National Institutes of Health, Public Health Service (C-3449), and the Damon Runyon Memorial Fund (DRG-352).

<sup>\*\*</sup>Research Fellow in Gynecologic Pathology.

### Materials and Method

Cases were selected from our files on the following basis: (a) the ovary should show no distortion by significant lesions; (b) only microscopic sections that appeared to be sagittal were considered.

The cases were collected until 10 specimens from each of the following periods of life were obtained: 21 to 30 years; 31 to 40 years; 41 to 50 years; 51 to 60 years; and 61 years and over.

Each slide (stained with hematoxylin and eosin) was placed in a 35 mm. projector by means of a cardboard holder. The section was projected on standard graph paper which was kept at a constant distance so that the magnification was always ×10.

The outline of the ovary was traced directly from the projected image to the graph paper. Next, all macroscopic structures were traced. The following structures could be identified during the projection: corpora albicantia, corpora lutea, hilum, cysts, clusters of vessels, artifacts, and stroma.

Of the 50 ovaries preliminarily selected from the surgical files, 20 were found to be suitable for tracing. These appeared to represent sagittal sections through the central portions of the ovaries.

Planimetrically, each tracing of these 20 specimens was then measured, recording the following: over-all area of each ovary, number of corpora albicantia, area minus artifacts and cysts, area of all corpora albicantia in each ovary, per cent of each ovary occupied by corpora albicantia, area of stroma, and average area of corpora albicantia.

#### Results

Table I shows no significant differences between the ovaries of pre- and postmenopausal women using these measurements.

Table I. Quantitative Relationships of Corpora Albicantia in Ovaries from 14 Premenopausal and 6 Postmenopausal Ovaries (Mean Values With Standard Errors)

	OVER-ALL AREA OF EACH OVARY (SQ. CM.)	NO. OF CORPORA ALBICANTIA	AREA MINUS ARTIFACTS AND CYSTS (SQ. CM.)	AREA OF ALL CORPORA ALBICANTIA IN EACH OVARY (SQ. CM.)	% OF EACH OVARY OCCUPIED BY CORPORA ALBICANTIA	AREA OF STROMA (SQ. CM.)	AVERAGE AREA OF CORPORA ALBICANTIA (SQ. CM.)
I.—Woman 42 years of age and younger	1.41 ±0.0913	7.57 ±1.57	1.29 ±0.0927	0.2014 ±0.0475	15.85 ±3.68	0.99 ±0.085	0.0288 ±0.00686
II.—Women 44 years of age and older	1.59	10.33	1.56	0.19	13.12	0.92	0.0235
	±0.226	±2.97	±0.224	±0.0538	±3.36	±0.0544	±0.00532
III.—(I vs. II)* ''t', ''p',	0.750	0.821	1.111	0.159	0.548	0.365	0.610
	0.5>p>0.4	0.5>p>0.4	0.3>p>0.2	0.9>p>0.8	0.6>p>0.5	0.8>p>0.7	0.6>p>0.5

\*"t" is the significance ratio. "p" is the probability of a greater value of "t." For example, 0.8>p>0.7 means that there is 70 to 80 per cent chance that difference under analysis is mere coincidence.

#### Comments

According to Taylor and associates<sup>6</sup> the earliest attempts at this type of examination were made by Henle and Sappy in 1873. These investigators were primarily interested in the number and size of follieles. Hoggstrom (quoted by

Taylor<sup>6</sup>), in 1921, and more recently Taylor and co-workers<sup>6</sup> completely examined ovaries by means of serial sections. Limits of time and resources make this type of evaluation unfeasible to us. Using our techniques, we cannot comment on the volumetric relationships of corpora albicantia to other structures in the ovary. Our two-dimensional planimetry should permit valid comparison of the relative amounts of corpora albicantia in different ovaries.

We are now in a position to speculate concerning certain apparent incongruities in the biology of corpora albicantia. There appears to be some method by which these structures are removed from the ovarian scene. Aside from the scientific interest in this problem, there is a practical aspect also. If some substance is aiding in the resorption of the corpora albicantia, this might become a useful therapeutic agent. Cicatricial tissue may respond to this material in other parts of the body such as in scarring of the face

The next phase of our study concerning the fate of the corpora albicantia will be directed along morphologic lines. We plan to re-examine the original slides of the ovaries using special stains. This may give us further information about the intrinsic structure of the corpus albicans and its relation to the surrounding ovarian stroma. We will also study the ovaries of fetuses and children in which no corpus albicans will be present. In addition, more complex histochemical procedures on ovarian tissue will be done.

## Summary

Hematoxylin and eosin-stained sections of ovaries from 14 premenopausal and 6 postmenopausal women were studied. Planimetric methods after image tracing on graph paper were employed to measure the corpora albicantia of these ovaries selected from our surgical files. No significant differences were found concerning the quantitative aspect of the corpora albicantia of pre- and postmenopausal women. The problem of the fate of the corpora albicantia formed during the reproductive life of a woman has been introduced.

The technical assistance of Mrs. Bette Anderson and Mr. James M. McCullagh is gratefully acknowledged.

#### References

- 1. Bancroft, H.: Introduction to Biostatistics, New York, 1957, Paul B. Hoeber, Inc., pp.
- Ham, A. W.: Histology, Philadelphia, 1957, J. B. Lippincott Company, pp. 759-775.
   Hertig, A. T.: J. Clin. Endocrinol. 4: 581, 1944.
   Schneider, G. T., and Bechtel, M.: Obst. & Gynec. 8: 713, 1956.
   Sommers, S. C., and Teloh, H. A.: A. M. A. Arch. Path. 53: 160, 1952.

- Sommers, S. C., and Teloh, H. A.: A. M. A. Arch. Path. 53: 160, 1952.
   Taylor, H. C., Jr., McAuley, P., and Engle, E. T.: In Engle, E. T., editor: Studies on Testis and Ovary: Eggs and Sperm, Springfield, Ill., 1952, Charles C Thomas, Publisher, pp. 140-155.

## THE REPAIR OF GENITAL PROLAPSE

GEORGE B. GIBSON, M.A., M.A.O., F.R.C.S.(Ed.), M.R.C.O.G., LURGAN, NORTHERN IRELAND

(From the Northern Ireland Hospitals Authority)

SURGICAL colleagues have a tendency to look upon genital prolapse as synonymous with gynecology. Though this is an exaggerated view it must be admitted that prolapse looms large in gynecological practice, particularly in communities where large families are traditional.

During a 3 year period from May, 1954, until April, 1957, I performed 610 repair operations. Since I did 639 other "major" operations, the repair operation represents almost half my operating experience during this period.

The series is not large but it has the advantage that it represents the work of a single operator using a standard technique. For this reason it may be profitable to review the problems which have been encountered and the results which have been obtained.

#### The Series

The operations were performed in 2 hospitals which serve an urban and rural area, including sections of 4 counties in Northern Ireland. This area has a population of approximately 180,000.

Age.—The age groups are shown in Table I. The percentages in each group correspond closely with those of Cox.¹ There were 276 patients (45.2 per cent) who had passed the menopause at the time of operation. No patient was considered too old for operation and, indeed, one of the most satisfied patients in the series was a diabetic, now aged 92, who had had a gross ulcerated procidentia for 20 years.

TABLE I. AGE GROUPS

AGE (YEARS)	NO. OF CASES	%
20-29	19	3.1
30-39	101	16.6
40-49	223	36.6
50-59	163	26.7
60-69	72	11.8
70-79	30	4.9
80-89	2	0.3

There were 32 patients over the age of 70 and a marked degree of disability had to be present before operation was advised. Preoperative assessment and preparation were more extensive than in younger patients and admission to the hospital was arranged at least a week before operation. The assessment included a chest x-ray examination, electrocardiography, and plasma protein estimation, and the preparation included sessions with the physiotherapist.

The youngest patient having a complete repair was 28, and 120 patients under 40 had some form of repair. Again, a greater disability was required as a prerequisite to operation in these younger patients. My records do not show how many patients were advised to postpone operation until symptoms became more pronounced or until the possibility of childbearing had passed. In all but the worst cases the effect of physiotherapy was studied before a decision was reached. Recently, pubococcygeus exercises, as recommended by Kegel, have alleviated some cases of stress incontinence which would previously have been subjected to operation.

Parity.—The parity of the patients is shown in Table II. Ten patients were nulliparous, all past the menopause. In parous patients, investigation of the obstetric history proved most unrewarding, particularly regarding operative interference, and I am inclined to agree with Pacey<sup>3</sup>: "too long has the poor old obstetrician been blamed for this disability." A personal impression is that an occipitoposterior position of the vertex is frequently responsible. This leads to delay in the first stage of labor, expulsive efforts due to impatience, and overstretching of the soft parts, even in the absence of operative interference.

TABLE II. PARITY OF PATIENTS

PARITY	NO. OF CASES	%
Nulliparous	10	1.6
1 to 3	287	47.1
4 and more	313	51.3

The Type of Prolapse.—Arthure and Savage<sup>4</sup> describe the 3 traditional degrees of uterine descent but they qualify their definition of the third degree in such a way that it could include cases where the uterus is not entirely outside the vulva. There were 507 patients in the series who had a Manchester repair and, as Table III shows, 4 degrees of uterine descent were recognized. In this classification, the determination was made when traction had been applied to the cervix during operation. The interpretation was as follows: first degree: the cervix descended slightly; second degree: the cervix reached the vulva; third degree: the cervix projected outside the vulva; fourth degree: the entire uterus was palpable outside the vulva.

TABLE III. DEGREE OF PROLAPSE

DEGREE OF PROLAPSE	NO. OF CASES	%
First	180	35.5
Second	178	35.1
Third	138	27.2
Fourth	11	2.2
Total	507	100.0

This method tends to place the degree of descent at its maximum value. However, only 11 cases (2.2 per cent) were of the fourth degree, emphasizing the comparative rarity of this condition.

An enterocele sac was recognized and dissected out in 36 of these 507 cases and it was overlooked in 3 additional cases, necessitating another operation.

Type of Operation.—Shaw<sup>5</sup> has written: "Looking back over a professional life of over half a century, no operation has rewarded me so well and so consistently as has the Manchester operation for genital prolapse. . . ." During my postgraduate training in the Queen's University, Belfast, I was

given a sound grounding in this operation and a lasting interest in it. I have seen no reason to depart from it during this series, though variations in the type of prolapse have led to modifications in individual cases, as shown in Table IV.

TABLE IV. TYPE OF OPERATION

OPERATION	NO.	OF	CASES
Manchester repair		50	)7
Anterior colporrhaphy		6	24
Amputation of cervix		1	15
Colpoperineorrhaphy			12
Anterior colporrhaphy and amputation of cervix			7
Amputation of cervix and colpoperineorrhaphy			6
Anterior colporrhaphy and colpoperineorrhaphy		9	36
Vaginal hysterectomy, anterior colporrhaphy, and colpoperineorrhaphy			3
Total		6:	10

Unlike in American series, 6-9 only 3 patients were treated by vaginal hysterectomy. In each case this was by chance rather than by planned operation. Each patient had a general prolapse of the fourth degree and an extremely atrophic uterus. Amputation of the cervix was performed, in error, at too high a level and the fragment of uterus which remained was not worth preserving as the keystone of the arch. Thirty-three additional repairs were excluded from the series because a vaginal hysterectomy was also performed. Hysterectomy was included in all these cases because of uterine anomalies, and was the primary operation. I feel that, far from contributing to the effectiveness of the repair, the hysterectomy detracted from it.

Technique of Operation.—The principles of the Manchester operation have been fully described by Donald, 10 Fothergill, 11, 12 and Shaw 13 and they need no further comment. There are many ways of applying these principles, however, and the minutae of technique are thought worthy of brief description. The steps are illustrated in Figs. 1 to 12 and are described below:

1. The anterior flap, roughly triangular, is shaped to suit the individual case. It is dissected from urethra to cervix, opening the vesicovaginal space. The edges are not undermined because excessive bleeding appears to outweigh any advantages to be gained from wide lateral dissection.

2. The bladder is separated from the cervix by gauze and sharp dissection until the vesicocervical pouch of peritoneum can be seen.

3. A layer of interrupted mattress sutures is inserted in the vesical fascia to invert the bladder wall and in the paraurethral fascia to narrow the lumen of the urethra and to strengthen the internal urethral sphincter.

4. The lateral cervical branches of the uterine artery are clamped and the cervix is amputated. The branches are ligated by sutures which also pass through the substance of the cervix.

5. The cervical stump is covered with mucosa by 4 Sturmdorf sutures, placed posteriorly, laterally, and anteriorly. These sutures include a considerable "bite" of the underlying endopelvic fascia and the anterior suture is so placed as to act as a Fothergill stitch. When the sutures are tied, the cervix should undergo considerable retroponation in the pelvis.

6. A layer of interrupted mattress sutures is inserted in the vaginal fascia. The needle is inserted beneath the cut edge in a lateral direction and parallel to the surface of the vaginal mucosa.

7. The anterior vaginal wall is closed by a continuous blanket suture.

8. The posterior flap dissection starts at the perineum and, in the last 2 years of the series, it has always extended to the cervix in order to avoid the missing of a potential enterocele.

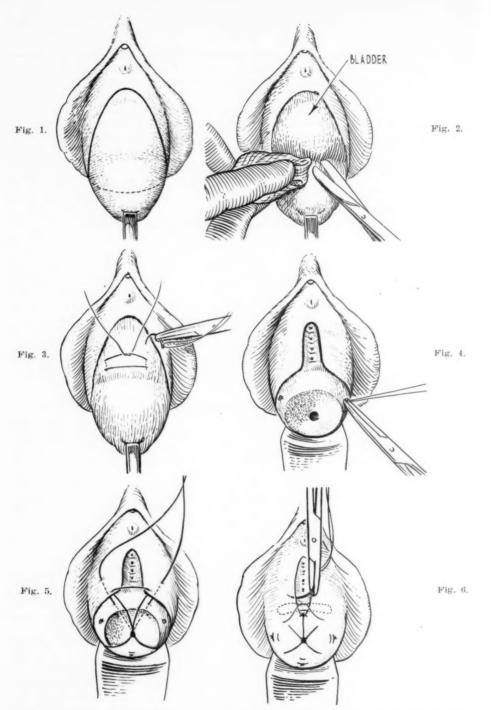


Fig. 1.—Third degree prolapse and the anterior incision which is continued around the  $\operatorname{cervix}$ .

Fig. 2.—Upward displacement of the bladder.
Fig. 3.—Layer of mattress sutures in vesical and paraurethral fascia. \*
Fig. 4.—The amputated cervix with lateral ligatures.
Fig. 5.—Reconstruction of cervical stump.
Fig. 6.—Layer of mattress sutures in vaginal fascia.

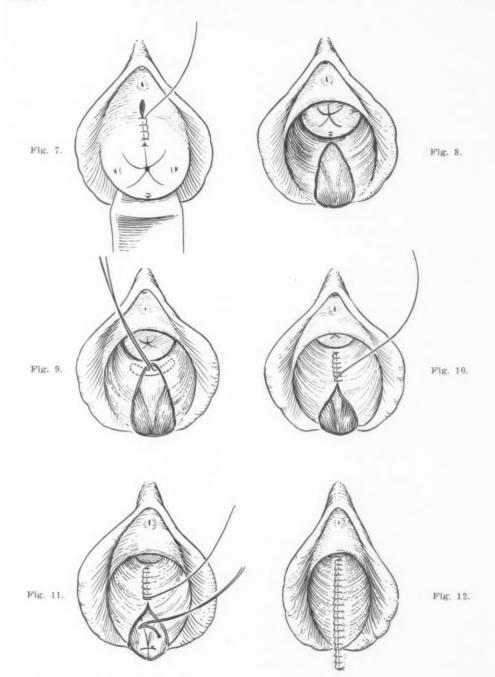


Fig. 7.—Closure of the incision.
Fig. 8.—The posterior incision.
Fig. 9.—Layer of mattress sutures in vaginal fascia.
Fig. 10.—Closure of the upper half of the incision.
Fig. 11.—Layer of sutures, reconstituting the perineal body.
Fig. 12.—Final closure of the incision.

9. A layer of interrupted mattress sutures is inserted in the vaginal fascia. The needle is again inserted beneath the cut edge in a lateral direction parallel to the surface of the mucosa.

10. The upper half of the posterior vaginal wall is closed by a continuous blanket suture, usually started before the deep sutures are tied. If access is difficult, it is more satisfactory to deal with the posterior repair in 2 stages, as recommended by Macafee. A triangular flap, apex upward, is removed from the upper half of the posterior wall, starting at the apex. When closure has been completed, as described, a second triangular flap is removed, starting at the base, on the perineum.

11. The levatores and and the superficial perineal muscles are united by interrupted sutures.

12. The remainder of the wound is closed by continuation of the blanket suture. Finally, a Foley catheter is inserted into the bladder and a plug is placed loosely in the vagina.

Operative Complications.—The only complications likely to be met during a repair are primary hemorrhage and injuries to adjacent viscera. It has been the practice to infiltrate the tissues with 30 ml. of 0.5 per cent lidocaine hydrochloride (Xylocaine) containing Adrenalin, 1 in 200,000; only one patient had a blood loss of sufficient severity to require a blood transfusion. There were no injuries to urethra, bladder, or ureter, but on four occasions the rectum was opened. In each case the opening was small; it was repaired at once, and the colpoperineorrhaphy was completed in the usual way. No postoperative enema was allowed and healing was uneventful.

Postoperative Complications.—These are detailed in Table V.

TABLE V. COMPLICATIONS

COMPLICATION	NO. OF CASES
Death	2
Secondary hemorrhage	16
Urinary infection	17
Wound sepsis	5
Thrombophlebitis	3
Pneumonia	1
Manic-depressive psychosis	1
Hematometra	1
Carcinoma in situ	1
Rectal fistula	1

Mortality: Phaneuf<sup>6</sup> has emphasized that, since prolapse is not a fatal condition, operative repair must have a very low mortality. He reported a mortality of 1.3 per cent in 1,066 cases. Gwillim<sup>15</sup> reported a mortality of 1.7 per cent in 405 cases, and Malpas<sup>16</sup> a mortality of 0.5 per cent in 3,753 cases between 1944 and 1953.

There were 2 deaths in this series, an incidence of 0.3 per cent, or, if only Manchester operations are considered, 0.4 per cent. Both patients had much in common. They were aged 58 and 59, respectively; both had a nulliparous procidentia, a severe degree of hypertension, and gross obesity. Both desired operation quickly, for personal reasons, so the usual practice of 6 months' preparation on a reducing diet was waived. In one case, death due to coronary thrombosis occurred 72 hours after operation, and postmortem examination showed no complication in the operative field. In the other case, death was due to a cerebral thrombosis on the twelfth postoperative day. An infected broad ligament hematoma, the only one in the series, may have contributed to the fatal outcome in the latter case, although the signs of this had subsided before the cerebral catastrophe occurred.

Secondary hemorrhage: As will be seen in Table V, 16 cases were complicated by secondary hemorrhage. The earliest occurred on the fifth day and the latest on the eighteenth day; the latter patient required readmission to the hospital. A hot douche, followed by the insertion of a vaginal pack, was sufficient to control the hemorrhage in 14 cases. The hemorrhage may well have been due to menstruation or to estrogen withdrawal. The remaining 2 cases were not controlled by the insertion of a pack. Examination under anesthesia revealed some disruption of the upper end of the anterior vaginal wound in each case and nylon sutures were inserted. Healing was delayed in one of these cases but the end result was satisfactory.

Infection: There were 17 cases of urinary infection, a diagnosis which was made if the patient developed urinary symptoms and/or if pus cells were present in abundance in the urine. The use of a Foley self-retaining eatheter for 72 hours after operation was much less arduous for patients and nursing staff than repeated catheterization. It must be added, however, that the incidence of infection increased from 1.8 per cent to 3.4 per cent if a Foley catheter was used (approximately 65 per cent of the cases). Five patients showed evidence of wound infection. One infection of a broad ligament hematoma has already been mentioned. Two others had purulent vaginal discharge and pyrexia, and 2 patients had to remain in the hospital more than the routine 13 postoperative days because of delayed healing of the perineum.

Among the conditions in which postoperative inactivity is a contributory factor, it will be noted that there were only 3 cases of thrombophlebitis, all mild, and one case of pneumonia; pulmonary embolism did not occur. This is attributed to early ambulation; all patients were allowed up on the day after operation. The sense of well-being resulting from this was a most valuable contribution to recovery and the practice did not appear to have a deleterious effect on the operative results.

Miscellany: One patient suffered a return of manic-depressive psychosis and had to be transferred to a mental hospital—she recovered within 4 months. Another patient developed a hematometra about a year after operation. There was no recurrence after dilatation of the cervix and the patient subsequently carried through a successful pregnancy.

There were 535 cases in this series in which the cervix was amputated. The cervix was always submitted for pathologic examination, and only one preinvasive carcinoma was detected. It is now 3 years since this diagnosis was made and there has been no evidence of recurrence. The association of the 2 conditions is stated to be rare but Funck-Brentano and associates<sup>17</sup> reported 5 cases of cervical carcinoma in association with procidentia. Rocker<sup>18</sup> reported a series of 449 cases of prolapse. There were 33 cases of procidentia and no less than 6 cases of carcinoma of the cervix in this group.

Finally, one patient developed a fecal fistula. After a straightforward operation, the postoperative stay in the hospital was uneventful. Sixteen days after discharge (29 days after operation) she developed mild pyrexia and pain in the perineum. Three days later fecal staining per vaginam commenced and this symptom persisted. A probe could be passed into the rectum through a small opening in the posterior vaginal wall, about one inch above the introitus. The fistula was closed by Vernon David's method 60 days after the repair operation. It is surprising that symptoms were so long delayed but it must be presumed that the rectal wall had been injured by one of the deep stitches.

Results of Operation.—A follow-up of cases is an undertaking of some magnitude and, for this reason, the review was limited to patients who had had a Manchester operation at least one year before the review started in May, 1957. This reduced the number to 345 and these patients were either

interviewed, interviewed and examined, or asked to reply to a comprehensive questionnaire, aided by their family doctor. Of the 345 cases, 338 were reviewed, a successful follow-up of 97.9 per cent. The cases of 7 patients were not reviewed. Two of these patients died as the result of the operation, 2 died before the review from causes unrelated to the operation, and every effort to trace the other 3 failed. At review an effort was made to ascertain the symptoms which were still present and to compare these with the symptoms which were present before the operation. The failure rate for each symptom was then calculated.

Before the results are considered, certain points should be emphasized. First, as leading questions were asked, this gave the maladjusted patient the opportunity to make the worst of her condition and subsequent examination sometimes failed to reveal any explanation for her symptoms. Second, a few patients developed symptoms after operation which were not present previously, so the failure rate is not strictly accurate. This applied particularly to urinary symptoms but it should be noted that no patient developed stress incontinence for the first time after operation. Last, and this tends to counterbalance the cases where symptoms are exaggerated or invented, there is no doubt that some patients omitted mention of symptoms, partly to spare the operator's feelings, and partly to avoid any chance of another operation.

The results of the review are shown in Table VI and each symptom will be considered in turn.

TABLE VI. REVIEW (338 OUT OF 345 POSSIBLE CASES)

SYMPTOMS	TOTAL BEFORE OPERATION	TOTAL AT REVIEW	FAILURE RATE
Backache	269	55	20.5
Prolapse	319	7	2.2
Discharge	190	15	7.9
Stress incontinence	243	25	10.3
Urge incontinence	162	38	23.4
Frequency	83	33	39.8
Bowel symptoms	128	17	13.3
Dyspareunia	_	34	_
Patients disappointed with result		17	5.0

Backache: This is a frequent complaint among women and has many causes, only one of which is prolapse. A failure rate of 20.5 per cent is lower than expected.

Prolapse: Fothergill<sup>12</sup> operated upon 156 patients between 1914 and 1916 and he had a 97 per cent cure rate. Held<sup>19</sup> dealt with 1,000 cases between 1940 and 1949. He reviewed 84 per cent of these and 94.7 per cent were cured. The failure rate in this series was 2.2 per cent and this appears to underline a view expressed earlier in this paper: that the Manchester operation is capable of giving good results in all cases of uterine prolapse. Of the 7 patients in whom the operation was considered a failure, 2 had a recurrence of cystocele, 2 suffered a recurrence of uterine prolapse after a subsequent confinement, and 3 had an enterocele which was overlooked at the original operation.

Discharge: Narrowing of the introitus and removal of an infected cervix should reduce the incidence of discharge, but there was a failure rate of 10.3 per cent. Most of the failures were due to vaginal infections, but, occasionally, an area of granulation tissue in the region of the cervical stump was the cause. Cauterization produced rapid amelioration in these cases.

Stress incontinence: Much has been written about this subject in recent years, and it was fully discussed at the Thirteenth British Congress of Obstetries and Gynaecology in 1952. At that congress, Aldridge<sup>20</sup> stated that a cure rate of 80 per cent was to be expected with a Kelly repair. Cox,¹ Pacey,³ and McLaren²¹ report better results. However, much depends on the interval, after operation, before the assessment is made and on the nature of the assessment. Bailey,²² in a searching investigation, reviewed the cases of 209 personal patients, 83 of whom had stress incontinence before operation. No patient developed stress incontinence as the result of the operation, but 51 of the 83 still had some degree of stress incontinence at the time of investigation.

It is difficult to know where to draw the line regarding this complaint. Nemir and Middleton<sup>23</sup> sent an anonymous questionnaire to 1,327 young nulliparas and found that 52.4 per cent occasionally suffered from stress incontinence, laughing being a more frequent precipitating factor than coughing. In a small personal investigation, on the same lines, I was unable to confirm this remarkably high incidence of stress incontinence.

I did find, however, that 18 of 169 young nulliparas did admit to stress incontinence (11 per cent) and, in the 52 who were over 25, the incidence increased to 20 per cent.

Although every effort was made in this review to examine all patients who complained of stress incontinence, I accepted the patient's assurance that she did not have this symptom. If every patient had been examined, care being taken to ensure a full bladder at the time of examination, the failure rate of 10.3 per cent may well have been increased. Another factor militating against a higher failure rate was the high incidence of stress incontinence before operation. Of the 507 patients who had a Manchester repair, 68.8 per cent admitted to some degree of stress incontinence. This is a much higher incidence than that recorded by Bailey<sup>22</sup>; milder cases must be included, and the cure rate should be correspondingly better.

In the limited number of cases in which another operation has been undertaken for the cure of this complaint, the method has depended on the anatomical result produced by the previous operation. If it was felt that this could be improved upon, another anterior colporrhaphy was performed. If not, the procedure described by Marshall, Marchetti, and Krantz<sup>24</sup> was used. I have found this operation simple, safe, and satisfactory in the small number of cases in which I have used it.

Urge Incontinence and Frequency of Micturition.—'A repair may improve these symptoms if they are due to chronic cervicitis or urinary stasis. There is always the risk, however, that operation will aggravate these symptoms. The results 2 years after operation were better than after one year, suggesting that the symptoms gradually subside.

Bowel symptoms: It is difficult to evaluate the bowel symptoms due to prolapse, but the most characteristic is a feeling, after defecation, that the rectum has not been completely emptied. No patient complained of this symptom at review; constipation was the usual complaint.

Dyspareunia: Solomons<sup>25</sup> reviewed the cases of 62 patients after repair and found that nine of these women (14 per cent) had severe dyspareunia. Thirty-four (10 per cent) complained of dyspareunia in this review. Some undoubtedly used the repair as an excuse, but others had reason for their complaint. The usual cause was a constriction in the middle third of the vagina, but one patient had an exaggerated fourchette, division of which cured her complaint.

# Summary

- 1. A personal series of 610 repair operations has been reviewed with reference to age, parity, type of prolapse, and type of operation.
  - 2. The technique of operation has been described.
  - 3. The operative mortality was 0.3 per cent.
- 4. Postoperative complications were minimal and this is attributed, in large measure, to the adoption of a practice of early ambulation in all cases.
- 5. A subsequent review of 338 cases was undertaken; this represented 97.8 per cent of the patients who had had a Manchester repair at least one year before review.
- 6. The effectiveness of the repair was considered in relation to each of the patient's symptoms and the most successful results were in the cure of the sensation of prolapse (97.8 per cent); the failure rate in stress incontinence was 10.3 per cent. Seventeen patients (5 per cent) were disappointed, in general, with the operative result.

Thanks are due to my anesthetists, Dr. W. Bingham and Dr. W. F. K. Morrow, for their constant interest in, and care of, these patients and to my nursing and medical staff, without whom this work could not have been undertaken. I am also indebted to Mr. G. A. Smith, medical artist, for his drawings and to the four County Medical Officers of Health, who supplied the population figures used in this study. Finally, I would like to express my thanks to Professor C. H. G. Macafee for his encouragement during this work and for his criticisms of my paper.

## References

- 1. Cox, L. W.: New Zealand M. J. 54: 330, 1955.
- Kegel, A. H.: J. Internat. Coll. Surgeons 25: 487, 1956.
   Pacey, K.: New Zealand M. J. 54: 322, 1955.

- Kegel, A. H.: J. Internat. Coll. Surgeons 25: 487, 1956.
   Pacey, K.: New Zealand M. J. 54: 322, 1955.
   Arthure, H. G. E., and Savage, D.: J. Obst. & Gynaec. Brit. Emp. 64: 355, 1957.
   Shaw, W. F.: Am. J. Obst. & Gynec. 68: 450, 1954.
   Phaneuf, L. E.: J. internat. chir. 13: 15, 1953.
   Hunt, W., and Counseller, V. S.: Surg. Gynec. & Obst. 99: 761, 1954.
   Taylor, E. S., McCallin, P. F., and Snow, R. H.: Am. J. Obst. & Gynec. 68: 428, 1954.
   Stearns, H. C.: West. J. Surg. 63: 420, 1955.
   Donald, A.: J. Obst. & Gynaec. Brit. Emp. 13: 195, 1908.
   Fothergill, W. E.: J. Obst. & Gynaec. Brit. Emp. 13: 410, 1908.
   Fothergill, W. E.: J. Obst. & Gynaec. Brit. Emp. 28: 251, 1921.
   Shaw, W. F.: Am. J. Obst. & Gynaec. 26: 667, 1933.
   Macafee, C. H. G.: Personal communication, 1948.
   Gwillim, C. M.: Proc. Roy. Soc. Med. 43: 973, 1950.
   Malpas, P.: Genital Prolapse and Allied Conditions, London, 1955, Harvey & Blythe, Ltd., p. 114. Ltd., p. 114.
- Funck-Brentano, P., Robert, H. G., and George, L. A.: Presse méd. 62: 539, 1954.
   Rocker, I.: J. Obst. & Gynaec. Brit. Emp. 65: 89, 1958.

- Rocker, I.; J. Obst. & Gynaec. Brit. Emp. 65: 89, 1958.
   Held, E.: Gynaecologia 133: 257, 1952.
   Aldridge, A.: J. Obst. & Gynaec. Brit. Emp. 59: 681, 1952.
   McLaren, H. C.: J. Obst. & Gynaec. Brit. Emp. 64: 673, 1957.
   Bailey, K. V.: J. Obst. & Gynaec. Brit. Emp. 61: 291, 1954.
   Nemir, A., and Middleton, R. P.: Am. J. Obst. & Gynaec. 68: 1166, 1954.
   Marshall, V. F., Marchetti, A. A., and Krantz, K. E.: Surg. Gynec. & Obst. 88: 509, 1949.
   Solomons, E.: Am. J. Obst. & Gynec. 70: 514, 1955.

# VASOPRESSIN AS A HEMOSTATIC IN GYNECOLOGIC SURGERY\*†

THOMAS F. DILLON, M.D., NEW YORK, N. Y.

(From the Departments of Obstetrics and Gynecology and Biochemistry of Cornell University Medical College and the New York Hospital (the New York Lying-In Hospital))

THE pressor-antidiuretic hormone of the posterior pituitary influences specifically the vascular tree and muscular elements of the genital tract.<sup>1, 2</sup> Its hemostatic effect has been utilized extensively over the years, but of late, the pressor-antidiuretic fraction has all but been discarded as a part of gynecologic surgery because of untoward side effects or incompatibility with anesthetic agents.<sup>2-5</sup>

The goal of this study is to investigate and re-establish hormonal hemostasis in gynecologic surgery. Observations on 20 patients constituted a preliminary report<sup>6</sup> from this clinic. This paper represents an extension of the previous report and presents data on the hemostatic effect of the pressor-anti-diuretic fraction of the posterior pituitary gland in varied gynecologic operations performed on 80 patients.

The isolation and synthesis of the principal hormone fractions of the posterior pituitary provided us with the compound vasopressin. Vasopressin is the name applied to the purified pressor-antidiuretic hormone isolated from the pituitary and its relationship to the commonly available commercial products of this series is depicted in Fig. 1.

We have indicated in Fig. 1 that vasopressin is the active principle pertinent to the purposes of this paper whether in Pitressin or in its purified form. Vasopressin and oxytocin represent the principal fractions of the posterior lobe. There is a possibility that another, as yet undiscovered, activity may exist.

Vasopressin, besides the pressor-antidiuretic activity, manifests a profound vasoconstrictive and strong contracting influence on the nonpregnant uterus.<sup>6</sup> This is in contrast to oxytocin wherein the stimulation of uterine contractions is greatest in the term pregnancy. Side effects that principally are constrictive phenomena involving the cardiovascular system must be attributed to vasopressin although what role the impurities may play is still unknown. Search of the literature indicates that these side effects are most often encountered when huge doses of one of the commercial preparations are used parenterally.<sup>4-6</sup>

<sup>\*</sup>Read at a meeting of the New York Obstetrical Society, Oct. 14, 1958.

†This work was supported by a grant (H1675) from the National Heart Institute of the Public Health Service and a grant-in-aid from Parke, Davis & Company.

## Material and Method

Thus, as indicated in our preliminary report, our study involved the use of the purified, natural, and synthetic vasopressin by *local* injection in small, dilute dosages, the purpose being to eliminate cardiovascular complications and to re-establish hormonal hemostasis in operations on or about the uterus.

We found that 4 units of vasopressin diluted in 20 ml. of saline resulting in 0.2 units per milliliter was effective. This volume of low concentration allowed for the diffuse local injection of small amounts throughout the operative area.

Our patients were selected, in that those above 45 years of age and those manifesting hypertension and/or cardiovascular disease were eliminated. The gynecologic condition was in no way selected. Anesthesia has been a combination of Pentothal, curare, nitrous oxide, and ether. In two cases Pentothal-cyclopropane induction with transfer to ether for the operative procedure was carried out. Our first 50 patients were monitored with continuous ECG recordings, a practice no longer considered necessary. Frequent, precise clinical

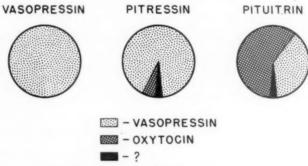


Fig. 1.—Posterior pituitary preparations.

observations were made and accurate blood loss tabulations were carried out by weighing sponges on a gram scale. A total of 80 patients have thus far been studied.

Myomectomy.—Vasopressin exerts maximum effect on the uterus itself and should therefore beneficially influence the operation of myomectomy. We have performed 39 myomectomies using vasopressin and 20 concurrent control operations of similar magnitude with no hemostatic agent.

The hormone is injected at the junction of the myoma or pedicle of the myoma with the uterus as illustrated in Fig. 2. The important feature is diffuse injection of the surrounding myometrium rather than of the myomas themselves. Depending on the size of the myoma, the initial dose is usually 10 ml. of the solution, or 2 units. This will last approximately 20 to 30 minutes, at which time, if bleeding recurs and/or more myomas are to be excised, repeat injection may be carried out. Arbitrarily, we have set 4 units as a maximum dose but, early in our study, we used 10 units in each of 2 patients and later, with very large tumors, we used 5 and 6 units, respectively, in 2 other patients.

The hemostatic influence does not affect or mask arterial bleeding. Arterial bleeding of significance remains visible and must be controlled with ligature.

The blood loss and the transfusion requirement have been significantly decreased as illustrated. Table I reveals the average number of units required per case. The average blood loss for the myomectomies in which vasopressin was utilized was 362 ml. as compared to 818 ml. for the controls.

TABLE I. MYOMECTOMY

4	CASES	UNITS	AVERAGE BLOOD LOSS (ML.)	AVERAGE BLOOD REPLACED (ML.)
Vasopressin	39	2.64	362	231
Control	20	0	818	725

TABLE II. TRANSFUSION REQUIREMENT IN MYOMECTOMY

BLOOD REPLACED (ML.)	VASOPRESSIN CASES (%)	CONTROL CASES
0	69.0	30.0
1 to 500	21.0	35.0
501 to 1,000	5.0	15.0
1,001 to 1,500	5.0	15.0
3,001 to 3,500		5.0

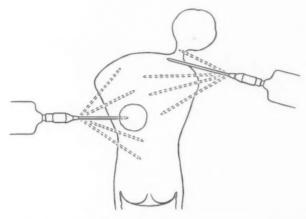


Fig. 2.—Diffuse local injection of vasopressin into myometrium surrounding myomas.

Table II shows the percentage of cases requiring blood transfusion. Sixtynine per cent of the vasopressin cases required no blood replacement as opposed to 30 per cent of the control cases. This figure is of statistical significance. The remainder of the cases required fewer units of blood within the vasopressin group.

The postoperative courses of the patients in the vasopressin group presented no major complication. Two instances of mild paralytic ileus were recorded. No instances of postoperative rebound bleeding requiring further operation were encountered. Similarly, there were no major complications among the controls. Two patients of the vasopressin group have successfully been delivered of normal infants thus far. Oxytocin and Pitocin utilized in 6 controls demonstrated no hemostatic effect.

Unification Operations.—Although unification operations<sup>25</sup> are infrequently done, it is in this procedure, perhaps, that vasopressin exerts its most visibly profound influence. The anomalous uterus is injected throughout as shown diagrammatically in Fig. 3.

The organ contracts and blanches as does the myomatous organ, resulting in virtually a bloodless operative field.

TABLE 111. UNIFICATION OPERATIONS

	CASES	UNITS	AVERAGE BLOOD LOSS (ML.)	AVERAGE BLOOD REPLACEI (ML.)
Vasopressin	5	3.56	194	0
Control	2	0	1.846	1,750

Table III provides the data for our series. Our general experience with this operation is reflected reasonably well in the 2 control cases within the study group. Unification operations have always been associated with excessive blood loss. Tourniquets and other mechanical methods do control bleeding but are often cumbersome and have not been used on our service for various reasons in myomectomy or unification operations. In this series, vasopressin effected a most dramatic control of blood loss and completely eliminated the need for transfusion. Parenthetically, it is important to note that the bloodless field

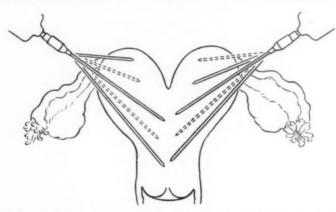


Fig. 3.—Diffuse injection of the anterior and posterior surfaces of anomalous uterus.

which results immeasurably simplifies the operative technique. The reduction in blood loss for this operation has made it inadvisable, in our opinion, to obtain more controls.

Invariably the effect of the hormone has disappeared within 30 minutes from the time of the last injection; the normal color and blood supply return well in advance of abdominal closure. There were no complications in this group of cases.

Anterior abdominal hysterotomy performed as part of certain tuboplastic operations is benefited exactly as are the unification operations. We have performed 3 such operations thus far with comparable reduction in blood loss.

Vaginal Operation.—The vasopressin solution has been utilized in several categories of vaginal surgery.

For cold knife conizations, <sup>26, 27</sup> 10 ml. containing 2 units is injected diffusely throughout the portiovaginalis of the cervix. Similarly, for cervical amputation<sup>28</sup> or preliminary to vaginal hysterectomy, <sup>29</sup> this same volume is placed diffusely within the cervix, beneath the reflection of the vaginal mucosa, and diffusely in the higher portions of the cervix and lower uterine segment as the dissection progresses (Fig. 4).

When anterior and posterior colporrhaphy are added to the above or carried out separately, an additional 10 ml. or 2 units may be diffusely injected submucosally throughout the anterior wall and the posterior wall immediately prior to dissection.

TABLE IV. CONIZATION OF THE CERVIX

	CASES	UNITS	AVERAGE BLOOD LOSS (ML.)	AVERAGE BLOOD REPLACED (ML,)
Vasopressin	11	2.13	46	0
Control	7	0	435	214

Table IV summarizes our experience in 11 cone biopsies and 7 controls. Cold knife conization of the cervix may result in surprisingly little or surprisingly great blood loss, a phenomenon that apparently depends upon the primary condition in the cervix. The control cases manifested blood losses ranging up to

yd

d

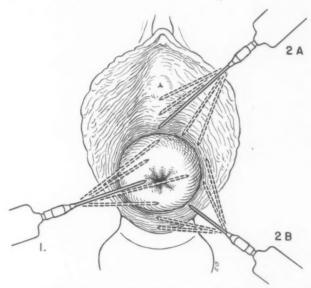


Fig. 4.—1, Complete injection of cervix for cone biopsy; 2A and 2B, areas to be injected for further operation.

1,200 ml. In the vasopressin group the blood loss ranged below 100 c.c. in the 11 cases and no transfusions were necessary. In both series the blood loss and the blood replaced refers to the time of the cone biopsy and does not include later operation that often was done.

In amputation of the cervix alone and in vaginal hysterectomy alone, our cases number only 2. We have done 5 vaginal hysterectomies with anterior and posterior repair in which vasopressin was used.

TABLE V. VAGINAL HYSTERECTOMY WITH REPAIR

	CASES	UNITS	AVERAGE BLOOD LOSS (ML.)	BLOOD REPLACED (ML.)
Vasopressin	5	3.4	457	200
Control	40	0	696	611
Adrenalin	5	0	270	0

Table V indicates that possibly the vasoconstrictive influence of vasopressin is of some benefit when compared to many more controls. The last line represents a control series of similar operations utilizing Adrenalin and procaine in

varying concentrations. These cases also reveal a significant reduction of blood loss, but each manifested a systemic response with increase in pulse and blood pressure to as much as 20 mm. Hg.

Table VI pertains to the Manchester operations that were carried out with and without vasopressin. The series is small but indicates the presence of the hemostatic influence.

TABLE VI. MANCHESTER OPERATIONS

	CASES	UNITS	AVERAGE BLOOD LOSS (ML.)	AVERAGE BLOOD REPLACEI (ML.)
Vasopressin	3	3.7	312	0
Control	12	0	857	833

Pitressin Series.—After obtaining our initial data with the purified hormone we began to use the slightly less pure commercial preparation, Pitressin. This product is much more readily obtainable and, if it would give the same effect, we would have the advantage of a compound readily available to all.

Utilizing the same dilution of 4 units in 20 c.c., we have now performed 12 operations utilizing Pitressin.

Table VII depicts our results with this preparation. This series is small but is comparable to the vasopressin group in results. The myomectomies, conizations, and one excision of the uterine septum reveal significant reduction in blood loss. The postoperative courses have been comparable to those in the vasopressin group.

TABLE VII. PITRESSIN OPERATIONS

CASES	OPERATION	UNITS	AVERAGE BLOOD LOSS (ML.)	BLOOD REPLACED (ML.)
7	Myomectomies	2.7	323	0
2	Conizations	3.0	85	0
1	Manchester	4.0	781	0
1	Amputation	2.0	40	0
1	Excised septum	2.0	83	0

# Side Effects

Purified vasopressin, synthetic vasopressin, and Pitressin manifested identical reactions. In general, the postoperative courses for both the control and the vasopressin-Pitressin group manifested a comparable number of minor complications, such as urinary tract infections. Intestinal obstruction and wound disruption were not encountered, although paralytic ileus of a mild degree was noted in both groups. The hospital stay was slightly longer in the control series; it was made so by isolated instances of prolonged, hectic postoperative courses. One patient from the control group was readmitted with homologous serum jaundice while 2 patients from the vasopressin series had a postoperative drop in hemoglobin which was never explained except by a rather weak attribution to laboratory error. In the entire vasopressin-Pitressin series there were no changes in blood pressure, pulse, or urinary output in any patient, and continuous electrocardiographic records in 50 of the patients were at all times normal.

#### Summary and Conclusions

1. Eighty gynecologic operations in which vasopressin and Pitressin were used as hemostatic agents are presented.

2. Vasopressin, whether purified natural or synthetic, exerts a hemostatic effect when injected locally into the nonpregnant uterus and perivaginal tissues. Commercially available Pitressin manifests similar activities of the same order of effectiveness.

3. The local injection of a dilute solution containing 4 units or less of the hormone effected decreased blood loss and diminution in the transfusion requirement as compared to the control groups.

4. No complications were encountered and no cardiovascular side effects were apparent in those patients who received vasopressin or Pitressin.

# References

- Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics: A Textbook of Pharmacology, Toxicology, and Therapeutics for Physicians and Medical Students, ed. 2, New York, 1955, The Macmillan Company.
   Moir, C.: J. Obst. & Gynaec. Brit. Emp. 57: 181, 1944.
   Mills, M., et al.: Proc. Staff Meet. Mayo Clin. 24: 254, 1949.

- Slotnik, I. L., and Teigland, J. D.: J. A. M. A. 146: 1126, 1951.
   Wakim, K. G., Denton, C., and Essex, H. E.: Am. Heart J. 47:
   Dillon, T. F., et al.: Obst. & Gynec. 11: 363, 1958. Am. Heart J. 47: 77, 1954.

- Dillon, T. F., et al.: Obst. & Gynec. 11: 363, 1958.
   Kamm, O., et al.: J. Am. Chem. Soc. 50: 573, 1928.
   Turner, R. A., Pierce, J. G., and du Vigneaud, V.: J. Biol. Chem. 191: 21, 1951.
   Popenoe, E. A., Lawler, H. C., and du Vigneaud, V.: J. Am. Chem. Soc. 74: 3713, 1952.
   du Vigneaud, V., Lawler, H. C., and Popenoe, E. A.: J. Am. Chem. Soc. 75: 4880, 1953.
   du Vigneaud, V., Ressler, C., and Trippett, S.: J. Biol. Chem. 205: 949, 1953.
   du Vigneaud, V., et al.: J. Am. Chem. Soc. 75: 4879, 1953.
   du Vigneaud, V., Gish, D. K., and Katsoyannis, P. G.: J. Am. Chem. Soc. 76: 4751, 1954.
   Bartlett, M. F., et al.: J. Am. Chem. Soc. 78: 2905, 1956.
   Mayo, W. J.: Surg. Gynec. & Obst. 34: 548, 1922.
   Bonney, V.: Lancet 1: 171, 1931.

ood

ood

ith

the

ne is we

12

all es, on he

i-

1e i-

d

e

ol

re

IS

1-

1

S

1-

0

- Bonney, V.: Lancet 1: 171, 1931.
   Bonney, V.: J. Obst. & Gynaec. Brit. Emp. 44: 1, 1937.
   Rubin, I. C.: AM. J. OBST. & GYNEC. 44: 196, 1942.
- 20. Rubin, I. C.: J. Mt. Sinai Hosp. 17: 565, 1950.
- Finn, W., and Muller, P. F.: AM. J. OBST. & GYNEC. 60: 109, 1950.
   Munnell, E. W., and Martin, F. W.: AM. J. OBST. & GYNEC. 62: 109, 1951.
- Davids, A. M.: AM. J. OBST. & GYNEC. 63: 592, 1952.
   Davids, A. M.: Surg. Clin. North America 37: 563, 1957.
   Strassman, E. O.: Obst. & Gynec. 10: 701, 1957.

- Fidler, H. L., Boyes, D. A., and Lock, D. R.: Canad. M. A. J. 77: 97, 1957.
   Williams, G. A., and Richardson, A. C.: Obst. & Gynec. 10: 60, 1957.
- 28. Gordon, C. A., and Gordon, R. E.: Am. J. Obst. & Gynec. 74: 392, 1957.
- 29. Waters, E. G.: Obst. & Gynec. 8: 432, 1956.

#### Discussion

DR. VINCENT DU VIGNEAUD (New York, N. Y.) .- The oxytocin that we have obtained from the hog, the cow, and the human have all seemed to be one and the same compound. On the other hand, the vasopressin from a hog differs from that from a cow. The commercial Pitressin may be either cow or hog, and I think mostly hog. All that the pharmacopeia requires is that it is an extract of edible animal. The hog vasopressin has the basic amino acid, lysine, and the cow vasopressin has arginine, another basic amino acid. Recently we analyzed the posterior pituitary from human pituitaries. It turned out to have the arginine vasopressin. I think most of the experiments you reported were with samples of arginine vasopressin, were they not?

DR. DILLON.—That is right.

DR. DU VIGNEAUD.—I think you have also done experiments with lysine vasopressin?

DR. DILLON.-That is correct.

DR. DU VIGNEAUD.—That seems to behave, unit for unit, about the same, although the pure lysine vasopressin seems not to be quite so active as the pure or highly purified arginine vasopressin on a weight basis.

# ABDOMINAL MENSTRUAL FISTULA\*

# Report of a Case and Review of the Literature

JOHN A. KIRKLAND, M.D., CHAPEL HILL, N. C.

(From the Department of Obstetrics and Gynecology, University of North Carolina, School of Medicine)

THE term "menstrual fistula" was first proposed by Ballin in 1928 for fistulas in laparotomy scars characterized by periodic discharge of blood, more or less coincident with normal menstruation. He considered two kinds of fistulas: (1) those due to direct communication with the uterine or tubal mucosa, and (2) those due to postoperative enclosures of endometrial tissue in the abdominal scar. In 1937, Maliphant proposed that the term "menstrual fistula" be confined to cases of the first type and since that time the term "fistula" has implied an actual connection between the uterine cavity and the opening of the abdominal wall. The enclosure of endometrial tissue in an abdominal scar has been considered a separate entity and is referred to as endometrioma, adenomyoma, or endometriosis is postoperative scars.

In this presentation we are concerned only with menstrual fistulas (i.e., the condition in which there is a communication between the uterine eavity and the abdominal wall). This may be by direct communication, a uteroabdominal fistula, or indirectly via the tube, a tuboabdominal fistula.

The following is a case of a uteroabdominal menstrual fistula which developed after a classical cesarean section, and was due to the presence of a foreign body.

D. S., NCMH 04-80-24, a 31-year-old white married woman, para 6-1-3-7, was first seen in the outpatient department of this hospital on Sept. 7, 1956, with the chief complaint of a discharge of dark blood through a lower abdominal scar occurring on three occasions since the birth of her last child by cesarean section on Feb. 27, 1956.

Information obtained from the patient and her attending obstetrician disclosed that she had an uneventful prenatal course and that she was admitted to another hospital on Feb. 23, 1956, at term, with ruptured membranes but not in labor. On Feb. 27, 1956, a classical cesarean section was done under spinal anesthesia for a compound presentation of a complete breech and right hand. A bilateral partial salpingectomy was also done at the request of the patient. Her postoperative course was complicated by separation of the skin edges with drainage from the wound, but the fascia was noted to be intact. She was discharged after 19 days, and 2 weeks following discharge a secondary closure of the wound was done under local anesthesia. The secondary closure finally healed by April 17, 1956. In May and June, at the time of her menstrual period, the patient noted some bluish swelling in the lower part of the abdominal scar and the escape of some dark

<sup>\*</sup>Supported in part by an Institutional Grant of the American Cancer Society.

of

or d, ds al ne ne y ne ed

dal

h a

st n-

n a n

of t.

e.

d

blood. Endometriosis of the abdominal wound was suspected by her physician, and on Aug. 16, 1956, under local anesthesia, this area of drainage in the lower abdominal wound was excised. The pathological report was that of sinus tract with acute and chronic inflammation of the skin and subcutaneous tissue. The incision healed well and the patient had no complaints until the time of her next menstrual period on Aug. 26, 1956, at which time she again had a bloody discharge from the lower part of the abdominal scar. She came to our outpatient department on Sept. 7, 1956, with this complaint and was followed there. On two different occasions, at the times of her menstrual periods in September and October, a bloody discharge from a small opening in the inferior portion of the abdominal scar was observed. The diagnosis of uteroabdominal menstrual fistula was made, and the patient was admitted for operation on Nov. 4, 1956. She had menstruated vaginally with each period in addition to the small drainage from the abdominal wound, and she had been asymptomatic otherwise.

Past medical and surgical history, review of systems, and family history were non-contributory.



Fig. 1.—Excised old scar, fistulous tract, and uterus. The fistulous tract and uterus have been opened and a probe is in the tract through the string material into the uterine cavity.

Physical examination on admission revealed a well-developed, well-nourished white woman in no distress. The only significant findings were on abdominal and pelvic examination. There was a lower midline abdominal scar, and in the inferior portion of the scar, approximately 7 cm. superior to the symphysis, there was a 0.5 cm. opening with serous drainage. The remainder of the scar was well healed. No masses were felt and there was no tenderness. On pelvic examination the external genitals and the vagina and

cervix were normal. The uterus was normal in size, anteflexed, and fixed to the anterior abdominal wall in the region of the cutaneous opening. Both adnexa were normal. Rectovaginal examination was normal.

Laboratory examination showed: hemoglobin, 13 Gm.; leukocyte count 8,000; urinalysis, normal; culture of the serous drainage from the opening in the incision revealed no growth. A hysterosalpingogram was unsuccessful in demonstrating the fistula.

The patient underwent operation on Nov. 5, 1956, under Pentothal sodium, cyclopropane, and nitrous oxide anesthesia. At operation a fistulous tract was demonstrated from the abdominal scar to the anterior portion of the fixed uterus. In the region of the fistula on the anterior surface of the uterus, a small wad of nonabsorbable cotton string was found, and the fistulous tract went directly through this area of cotton material. The exact nature of the material could not be ascertained but it was thought to be a foreign body rather than nonabsorbable suture material. An excision of the abdominal scar and the fistulous tract, a total abdominal hysterectomy, a left salpingo-oophorectomy, and right salpingectomy were performed. The patient tolerated the procedure well. Her postoperative course was uncomplicated except for mild atelectasis, and she was discharged on the tenth postoperative day in good condition.

The pathology report of the specimen described a fistulous opening in the scar in direct continuity with the anterior superior portion of the uterine cavity in the region of the nonabsorbable string foreign body (Fig. 1). The fistulous tract was lined by granulation tissue, by chronic inflammatory cells including many hemosiderin-filled macrophages, and by a few foreign body giant cells.

The patient did well postoperatively, was followed in the gynecology clinic, and was last seen 6 months following operation, at which time the abdominal wound was well healed and the patient was asymptomatic.

The final diagnosis was uteroabdominal menstrual fistula due to nonabsorbable foreign body following classical cesarean section.

#### Comment

Reports in the literature of abdominal menstrual fistulas are infrequent. Ballin¹ stated that up to 1928 about 40 cases had been reported in the literature in which a menstrual fistula was due to a communication with the uterine cavity. At least 32 of these followed cesarean section, and the remainder followed a variety of pelvic operations, including salpingectomy for pelvic inflammatory disease, myomectomy, and ventral fixation. Rarely one followed the spontaneous rupture of a pyosalpinx or tubal pregnancy. Since 1928 there have been, including the present case, reports of, or reference made to, 58 additional cases of menstrual fistula, bringing the total to almost 100 cases. The case reports in the accessible literature since 1928 have been reviewed, but in only 33 have there been sufficient data to make an analysis.

These menstrual fistulas are almost always formed postoperatively, preceded by various operations. Fifteen<sup>1, 3-16</sup> followed laparotomy in which pelvic inflammatory disease was found and in which either a salpingectomy or salpingo-oophorectomy was done. Seven followed cesarean section, 6<sup>17-19</sup> of which were classical sections and one<sup>20</sup> a low transverse transperitoneal section. Four<sup>1, 21, 22</sup> followed fundectomy or myomectomy, and in all a salpingectomy was done also. Two<sup>23, 24</sup> followed appendectomy alone and 2<sup>2, 25</sup> followed incision and drainage of a pelvic abscess which pointed to the inguinal region. Ventral suspension of the uterus<sup>15</sup> and inguinal herniorrhaphy in which a pyosalpinx was in the sac<sup>26</sup> each preceded the formulation of the fistula in one case. One fistula<sup>27</sup> was caused by the spontaneous rupture of a tuberculous abscess in the inguinal region.

The fistulas that developed were of two types. In the first were those in which there was a direct communication between the uterine cavity and

nec. 959

ior

to-

ari-

led

elo-

ted

the

ing

ial.

a

nal

ny, Ier

lis-

in

ion

by

ro-

ras

ell

or-

nt.

a-

ne

er

ed

re

58

es.

d.

·e-

eh

ny

al

a

nd

he

ni-

a-

us

se

abdominal wall (i.e., a uteroabdominal fistula). Twenty-two were in this group, following cesarean section, myomectomy or fundectomy, ventral suspension, or salpingectomy in which the tube was resected down to the cornua. In these the uterus was adherent to the anterior abdominal wall, and the fistula passed directly into the uterine cavity. In the second group the communication between the uterus and the abdominal wall was indirect via the Fallopian tube or tubal stump (i.e., a tuboabdominal fistula). Eleven of the cases presented this type of fistula and followed partial salpingectomy in which a tubal stump remained, or other abdominal procedures in which the Fallopian tubes were left intact, such as appendectomy and incision and drainage of an abscess. In addition to the fistulous connection to the abdominal wall, infrequently there may be an associated intestinal fistula and along with the periodic discharge of blood, there may be fecal drainage. This was present in 4 cases.<sup>1, 3, 27</sup>

Several associated factors played an important part in the etiology of the Infection played a major role in the formation of both types of fistulas. In 26 of the cases either the primary operation was for an inflammatory process, there was a postoperative wound infection, or the patient ran a febrile course. Also of interest is the fact that in the 14 years prior to 1942, 24 of the 33 cases were reported, and in the 14 years after 1942, only 9 cases were reported. The year 1942 corresponds roughly to the introduction of antibioties; therefore, the use of antibioties has undoubtedly reduced the number of fistulas, particularly in cases where operation was performed for an inflammatory process. Drainage, either by gauze packing of the wound or by rubber drains, was mentioned in 12 cases, and the fistulas in these cases developed in the drainage site. A gauze tampon was found in the abdominal cavity in the region of the fistula in one case following a salpingectomy for pelvic inflammatory disease, and nonabsorbable suture material was present in the wall of the uterus in 2 cases following cesarean section. 18, 19 In the present case report, a nonabsorbable foreign body was the main contributing factor in the formation of the menstrual fistula. In 16 cases of menstrual fistula reported from the Mayo Clinic in 1928 by Masson and Simon,<sup>28</sup> non-absorbable suture material was present in 3, and inflammatory disease in all cases. The mechanical factor of hematometra played a part in 2 cases. In one,4 the patient had an amputation of the cervix, amenorrhea, hematometra, and development of a menstrual fistula following a salpingectomy 4 years later. The other12 was an unusual case of hematometra in an isolated rudimentary cornu and the development of the fistula following a salpingectomy on that side. Thus, pelvic or wound infection, drainage, the use of nonabsorbable suture material, the presence of a foreign body, and mechanical blockage of the normal path of menstruation may all play a part in the formation of a fistula, in the direct type, causing adherence of the uterine wound to the parietal wound, and, in the indirect type, causing adhesion and fixation of the fimbriated end of the Fallopian tube or the tubal stump to the abdominal wall. The development of a fistula in the presence of infection, when drainage is used, and when nonabsorbable suture or a foreign body is found, is readily explainable. The development of a fistula in the absence of these factors may be caused by direct or indirect involvement of the uterine mucosa in which the mucosa may grow from the uterine cavity or from ectopic mucosa of the tubal stump by continuous invasion to the cesarean section or laparotomy sear. Growth from the mucosa of the tubal stump was proposed by Sampson<sup>29</sup> as the pathogenesis of postsalpingectomy endometriosis in laparotomy scars, and fistulas may well develop in these tracts of ectopic mucosa to form menstrual fistulas. The isolation of the

mucosa of the uterine cavity in closing, careful suturing, and adequate peritonization will aid in preventing this sequence of events. The formation of a fistula without previous operation is extremely rare. One case<sup>27</sup> in this series occurred following the spontaneous rupture of a tuberculous pelvic abscess into the inguinal region. Ballin¹ also reported one similar case and also a case of a fistula following the spontaneous rupture of a tubal pregnancy through the abdominal wall.

The diagnosis does not usually present a problem. There is usually a history of a previous pelvic operation and the chief complaint is a dark, bloody discharge from the sear at the time of menstruation. In addition to the characteristic bloody discharge from the fistulous opening in the abdomen which was present in all 33 cases, the patient may complain of a serous drainage in between periods. At the time of menstruation, the actual bleeding may be preceded by some pain in the region and the presence of a lump or bluish swelling which ruptures concomitantly with the onset of bleeding. The average age of the 33 patients was 30 years, ranging from 18 to 55. The interval between operation and the presence of the fistula ranged from immediately with the first menstrual period to as long as 16 years after a laparotomy for pelvic inflammatory disease. The majority developed within the first year.

Endometriosis in a postoperative scar must be considered in the differential diagnosis. In a review of 31 cases of this condition, Wyrens and Randall<sup>30</sup> reported antecedent operations similar to those which precede a menstrual fistula. The most common symptom in these cases was a painful, tender nodule at the time of menstruation, but in 4 cases there was periodic bleeding from the scar. Therefore, with a similar history and physical findings, it is important from the standpoint of appropriate surgical treatment to attempt to demonstrate an actual fistula to the uterine cavity and to differentiate it from endometriosis within the scar.

Demonstration may be by the injection of dye into the opening and its appearance in the cervix, which was done in 3 cases, 2, 9, 26 or by hysterosal-pingogram, which demonstrated the fistula successfully in 97, 8, 10, 11, 13, 15, 16, 24, 27 of the cases reviewed.

Spontaneous healing of a menstrual fistula is rare, and an operation is usually required. Two of the 33 fistulas reviewed healed spontaneously. One6 was treated with a dilatation and curettage, which stopped menstruation for 9 months, and scraping and cauterization of the fistulous tract, which resulted in spontaneous closure. Another closed spontaneously, being treated only with a large catheter in the cervix to facilitate drainage. Operative treatment may consist of excision of the fistulous tract alone, which was done in 19 cases with one recurrence, or of excision of the tract plus hysterectomy, which was done in 12 cases with no recurrence. When childbearing in a young woman is a consideration, excision of the tract with preservation of the uterus is the operation of choice. If the tract communicates with the uterus through either Fallopian tube or tubal stump, a salpingectomy should be performed. If the fistula leads directly into the uterus, the intramural portion of this tract should also be removed and the uterus carefully closed. In patients rendered sterile either by infection or by previous surgery or in older women in whom further pregnancies are not a consideration, excision of the tract plus a total abdominal hypsterectomy is the procedure of choice.

#### Summary

A case is presented of uteroabdominal menstrual fistula following a classical cesarean section and due to a foreign body. Thirty-three cases of menstrual fistula reported since 1928 are reviewed.

nla

C-

to 98 h

a

P-

h

n 90 h 1il

T

d a l,

C 1-

0 .

-

6

d y 9 h 5 S h

S S

#### References

- Ballin, M.: Surg., Gynec. & Obst. 46: 525, 1928.
   Maliphant, R. G.: Lancet 1: 1509, 1937.

- 3. Mesa, C.: Semana méd. 1: 23, 1929. 4. Drips, D. G.: M. Clin. North America 12: 1577, 1929. 5. Brady, L.: Bull. School Med. Univ. Maryland 15: 73, 1930.
- Tortora, M., and Sanvitale, A.: Rassegna d'ostet. e ginec 39: 163, 1930.
   Molfino, A. H., and Boero, R. A.: Semana méd. 2: 1152, 1932.
   Swigart, W.: Zentralbl. Gynäk. 57: 458, 1933.
- 9. Rizzo, G.: Policlinico (sez. prat.) 41: 1056, 1934. 10. Wimpfheimer, S.: AM. J. OBST. & GYNEC. 34: 146, 1937.
- 11. Palmer, R., and Pulsford, J.: Bull. Soc. gynéc. et d'obst. 27: 63, 1938. 12. Kraul, L.: Wien. med. Wchnschr. 51: 759, 1938.

- Kraul, L.: Wien. med. Wchnschr. 51: 759, 1938.
   Todd, T. F.: Proc. Roy. Soc. Med. 32: 1590, 1939.
   Schunke, G. B., and Waugh, J. M.: Proc. Staff Meet. Mayo Clin. 16: 664, 1941.
   Ernst, M. A.: Bol. Soc. chilena de obst. y ginec. 11: 20, 1946.
   Chigot, P. L., and Weschler, R.: Presse méd. 56: 684, 1948.
   Price, J. W.: Kentucky M. J. 26: 475, 1928.
   Devraigne, L., Banzet, P., and Mayer, M.: Bull. Soc. gynéc. et d'obst. 19: 403, 1930.
   Vermelin, H., and Louyot, J.: Soc. d'obst. et d'gynéc. de Nancy 3: 463, 1951.
   Nogueira, I. P.: Rev. de ginec. e d'obst. 1: 368, 1943.
   Schauffer, G. C.: Northwest Med. 28: 399, 1929.
   Salaber, J. A., and Nogues A. E.: Bol. Soc. de obst. y ginec. de Buenos Aires 26:

- 22. Salaber, J. A., and Nogues, A. E.: Bol. Soc. de obst. y ginec. de Buenos Aires 26: 332, 1947.
- Conrad, G.: Fortsch. d. Med. 47: 393, 1929.
   Moura, P., and Ribeiro, F.: Rev. de ginec. e d'obst. 30: 141, 1936.
   Bello, E.: Rev. med. peruana 9: 489, 1937.

- 26. Jeanneney, G., and Laporte, F.: J. de méd. de Bordeaux 109: 415, 1932. 27. Kinnunen, O.: Acta obst. et gynec. Scandinav. 29: 197, 1949. 28. Masson, J. C., and Simon, H. E.: AM. J. OBST. & GYNEC. 16: 682, 1928.
- Sampson, J. H.: Am. J. OBST. & GYNEC. 50: 597, 1945.
   Wyrens, R. G., and Randall, L. M.: Am. J. Surg. 56: 395, 1942.

# LYMPHOCYST FORMATION FOLLOWING PELVIC LYMPHADENECTOMY\*

JAMES H. NELSON, JR., LIEUTENANT (MC) USN, AND J. WILSON HUSTON, CAPTAIN (MC) USN

(From the Department of Obstetrics and Gynecology, U. S. Naval Hospital, St. Albans, N. Y.)

THE purpose of this paper is to report 2 cases of lymphocysts developing in the region of the iliac vessels following pelvic lymphadenectomies. Gray and associates¹ recently made the first report on this in the American literature. The greatest experience with this troublesome complication, however, has been reported in the Japanese literature. The initial report confined to this subject was that of Kobayashi² in 1950. In 1955 Mori³ reviewed the subject in an attempt to evaluate etiological factors.

At St. Albans Naval Hospital, since 1952, there have been 33 patients with carcinoma of the cervix treated by pelvic lymphadenectomy. Eight of those 33 patients had received preoperative radium therapy.

# Case Report

Case 1.—Mrs. E. A. W., a 36-year-old para 3-0-1-3, was well until October, 1954, when she was seen at an Air Force Dispensary in Alaska with a complaint of metrorrhagia of one month's duration. The recurrence of the bleeding in November prompted her admission to the hospital in Alaska where a dilatation and curettage and cervical biopsy were performed on Dec. 2, 1954. A diagnosis of invasive carcinoma of the cervix was made and the patient was transferred to the United States for therapy.

Past History.—Except for a cholecystectomy and appendectomy, the past history was otherwise within normal limits. A review of systems was noncontributory.

Physical examination was within normal limits except for pelvic examination. The cervix was markedly eroded with induration extending into the left lateral fornix. The cervix was, however, mobile; the fundus was normal in size and freely movable; the adnexa were palpable and normal. The lesion was classified as a League of Nations Stage II.

Course.—On Feb. 14, 1955, a radical hysterectomy and bilateral pelvic node dissection were carried out. The postoperative course was uncomplicated and the patient was discharged on the ninth postoperative day. On follow-up examination, April 18, 1955, the patient had developed bilateral cystic masses which increased in size perceptively. She was re-admitted to the hospital on April 19, 1955, and a laparotomy was performed on April 22. At laparotomy, the abdomen was found to be within normal limits and was free of any suggestion of metastatic disease. Lying along the right pelvic wall, extraperitoneal, was a soft cystic mass approximately 4 cm. in diameter and 12 to 15 cm. long. On the left lateral pelvic wall was a similar mass much smaller measuring approximately 3 by 4 cm. The pelvis was otherwise free of disease. At the time of operation, the peritoneum was incised over the large mass on the right and dissection continued until a clear yellow serous fluid drained

<sup>\*</sup>The opinions expressed are those of the authors and do not necessarily reflect the views of the Navy Medical Department.

ND

d

1e

e-

et t-

h

en ie io d

18

e

d

d

1

n

e

from the mass. The area was then unroofed and found to be a large irregular cavity lined with a thick gray membrane and was thought to be a lymphocyst (Fig. 1). The smaller mass on the left side was similarly unroofed and was found to contain the same type of fluid. It was lined by a similar type of membrane. These areas were left opened and the abdomen closed in layers. The patient recovered uneventfully and was discharged to the Tumor Clinic on the seventh postoperative day. She has been followed in the Tumor Clinic and is well  $3\frac{1}{2}$  years postlymphocystotomy with no evidence of recurrent disease.

Case 2.—Mrs. M. G., a 38-year-old para 0-0-0-0, was first admitted to this hospital in July, 1957, at which time a diagnosis of invasive squamous cell carcinoma of the cervix was made. On Aug. 5, 1957, a radical hysterectomy and pelvic node dissection was done. Post-operatively, the patient developed a vesicovaginal fistula. On Sept. 9, 1957, a mass was felt in the left pelvis.

Physical Examination.—Findings were limited to the pelvis where the fistula was visible on the anterior vaginal wall. The mass was palpable as described above.

Laboratory Data.—Hemoglobin, 15.0 Gm. per cent; hematocrit, 46 volumes per cent; white blood count, 6,500. Urine showed white blood cells too numerous to count. Culture revealed a proteus.

Hospital Course.—On Nov. 23, 1957, an exploratory laparotomy was carried out revealing a peritoneal cyst of the left obturator fossa. The cyst measured approximately 6 cm. and



Fig. 1.—Photograph taken at time of laparotomy in Case 1, showing the opened lymphocyst on the right side of the pelvis.

was filled with a watery straw-colored fluid. The cyst was unroofed and left open. At that time an attempt was made to close the fistula but on the twelfth postoperative day the patient began leaking again. In April, 1958, a second attempt was made to close the fistula vaginally and was successful.

The patient was last seen at follow-up on June 1, 1958, with no recurrence of the cystic mass in the pelvis and no recurrence of the vesicovaginal fistula.

## Comment

The report by Gray and co-workers included 9 cases, all of which followed full courses of radiation therapy. That report did not clarify the question of whether this complication occurred in nonradiated cases or whether their

attack on cervical cancer always includes radiation therapy. At any rate, their incidence was 9 cases in 55 patients, or 16.3 per cent. Clinically, 4 of the 9 cases reported had morbidity attributable directly to the lymphocysts.

Mori reported 68 instances of lymphocysts out of 140 cases, or 48.5 per cent, who had the Okabayashi operation. His cases were unrelated to radiation therapy since an insignificant number were given radiation. Clinically, Mori speaks of the lymphocyst as a benign collection of fluid, which gives no symptoms unless it is infected or reaches a very large size when it will cause edema of the lower extremity. The 2 cases reported here reflect the experience of Mori in that neither patient had any symptoms associated with these cysts. Instead, their presence was discovered on routine follow-up examination.

Mori describes the lymphocyst as occurring between the tenth and twentieth postoperative days. Gray states 1 to 6 months following operation as the time of occurrence of this complication. In the present series the cysts were first noted on the sixty-third and thirty-fifth days, respectively. Mori made a thorough investigation into the problem and found a correlation between the incidence of cyst formation and the total number of nodes removed. He also found that the amount of removed tissue surrounding the extirpated nodes correlated with the cyst formation. Thus Mori was led to the conclusion that the more radical the operation the higher the incidence of cyst formation.

Both cases reported here were managed by exploratory operations and unroofing the cysts. However, in cases where infection is not a problem and where the cysts do not obstruct the circulation in the lower extremity by their mere size, it would seem to be wiser to wait and watch the cysts for regression. Both Gray and Mori found spontaneous regression to be the usual course in the majority of cases. It is important to point out that the cases presented here are not comparable to those presented by Gray where courses of x-ray and radium therapy had been given.

#### References

Gray, M. J., Plentl, A. A., and Taylor, H. C., Jr.: Am. J. Obst. & Gynec. 75: 1059, 1958.
 Kobayashi, T., and Inone, S.: Clin. Gynec. & Obst. 4: 91, 1950.

<sup>3.</sup> Mori, N.: J. Jap. Obst. & Gynec. Soc. 2: 178, 1955.

# SUPERIOR MESENTERIC SYNDROME FOLLOWING PELVIC INFLAMMATORY DISEASE

Report of a Case

e

у,

10

e

S.

ıie

le

0

S

it

1d

ir

1.

n

d

GEORGE H. HADDAD, M.D., AND WAYNE H. DECKER, M.D., NEW YORK, N. Y.

(From the Departments of Surgery and Gynecology of the Knickerbocker Hospital)

THE superior mesenteric syndrome is a condition that manifests itself by signs and symptoms of partial or complete obstruction of the third portion of the duodenum.<sup>4</sup> Usually, it is a complication of a developmental anomaly of the midgut. However, the syndrome can and does occur from a variety of other causes that might produce tension of the superior mesenteric vessels and thus compress the transverse portion of the duodenum.<sup>5</sup>

Dott¹ gave a lucid depression of the sequence of intestinal rotation and its surgical significance. Intestinal rotation is divided into 3 major stages. In the first stage, the midgut occupies the umbilical cord and a 90 degree counterclockwise rotation occurs. In the second stage, the midgut completes the 270 degree counterclockwise rotation and is reduced into the abdominal cavity, the cecum resting in the vicinity of the right loin. The third stage consists of farther descent of the cecum to the right iliac fossa and fixation of parts of the intestines to the posterior abdominal wall by fusion of their mesentery with the posterior parietal peritoneum. This results in the relationship and attachment of the bowel as seen in a normal adult. Arrest may occur at any stage described above.

The case being presented here had an arrest in the third stage, namely, complete lack of attachment of the midgut to the posterior abdominal wall.

Acute pelvic inflammatory disease which results in pelvic peritonitis is not uncommon. These patients frequently develop intestinal obstruction due to paralytic ileus. Intestinal intubation and appropriate measures to combat the inflammatory process usually result in relief of peritonitis and restoration of intestinal activity. The following case report is of interest in this regard.

K. H., No. 756369, a 43-year-old Negro woman, was admitted to the gynecology department because of severe lower abdominal pain of one day's duration. The pain developed suddenly, was sharp and constant, and radiated to the lower back. There was moderate vaginal discharge. Temperature on admission was 100.7° F. Physical examination revealed tenderness in the lower abdominal quadrants and muscle guarding. A midline suprapubic sear of an old operation was present. (In 1939, she had an oophorectomy and appendectomy.) On pelvic examination, there was tenderness in the adnexa and an indefinite mass was felt on the left. The white blood count was 20,000 with a differential of 87 per cent polymorphs; 11 per cent lymphocytes, and 2 per cent monocytes. A diagnosis of acute pelvic

inflammatory disease, tubovarian abscess, and pelvic peritonitis was made and treatment with antibiotics instituted. On the second day, she vomited once. The physical findings remained unchanged. In the following days, she vomited, intermittently, dark, green fluid, and a nasogastric tube was inserted. The physical findings on abdominal examination fluctuated from day to day with increasing and decreasing abdominal distention. The tenderness in the lower quadrants was the only constant finding. She continued to pass flatus in small amounts. On the sixth day of admission she became moderately interior. Vaginal examination again revealed a tender indefinite mass; this was aspirated through the vaginal vault but nothing was recovered. X-ray films of the abdomen showed a distended intestinal loop with a fluid level in the right upper quadrant. She continued to drain large quantities of dark

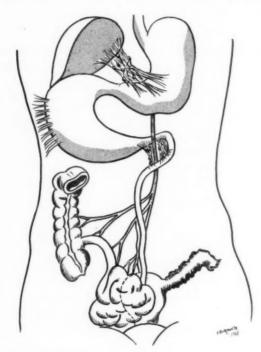


Fig. 1.—Semidiagrammatic presentation of the findings at operation as described in the text.

green fluid through the nasogastric tube. Serum bilirubin was 5.9 mg. per cent; alkaline phosphatase 5.9 Bodansky units; cephalin flocculation negative. A diagnosis of high intestinal obstruction was made and laparotomy performed.

At operation it became evident that the obstruction was high because all the small bowel was collapsed and, as a result of recent pelvic inflammatory disease, matted together and adherent to all the pelvic organs (Fig. 1). The right Fallopian tube, ovary, and appendix were absent. The left Fallopian tube showed evidence of recent acute salpingitis. It was moderately swollen and congested and its surface was covered with fibrinous exudate.

Regressing peritonitis was apparent over almost all the bowel and the surface of the liver. The stomach and duodenum were distended, the duodenum was enlarged to almost the size of a normal stomach. The exact site and cause of the obstruction could not be ascertained until all the small bowel was freed from the pelvis. Only then did it become evident that there was a total lack of mesenteric fixation of the small and proximal large bowel. The superior mesenteric vessels<sup>2</sup> were stretched tight and compressed the third portion of the duodenum. A thick narrow congenital band bridged the duodenojejunal loop. A similar but

ent

reid.

uc-229

all

on

out

a

rk

ne in-

rel nd ix as

he he ernt he he ut much wider band stretched from the descending portion of the duodenum to the lateral abdominal wall. Thinner adhesive veils covered the anterior surface of the stomach to the porta hepatis and were distinct from the gastrohepatic omentum. Multiple large lymph nodes were present in the gastrohepatic omentum and a few scattered ones in the small bowel mesentery.

The above-described bands were cut and several small bowel adhesions freed, releasing the tension of the superior mesenteric vessels. The lumen at the duodenojejunal junction was quite adequate and decompression of the distended duodenum resulted. No short-circuiting procedure3, 5 was deemed necessary or advisable in the face of peritonitis. A biopsy specimen of the liver was obtained.

Postoperatively, the patient made an uneventful recovery. The jaundice gradually subsided and the serum bilirubin was normal at the time of discharge. The biopsy of the liver showed biliary stasis only. The patient was asymptomatic and eating a regular diet when discharged on the seventeenth postoperative day.

# Summary

The stages of intestinal rotation and mesenteric fixation are outlined. A case of superior mesenteric syndrome resulting from acute pelvic inflammatory disease and congenital absence of mesenteric fixation is presented.

## References

- Dott, N. M.: Brit. J. Surg. 11: 251, 1923.
   Waugh, G. E.: Brit. J. Surg. 15: 438, 1928.
   Kellogg, E. L., and Kellogg, W. A.: Ann. Surg. 73: 578, 1921.
   Robinson, B.: Cincinnati Lancet-Clinic 45: 577, 1900.
   Roodenberg, A. I., and Bodon, G. R.: New York J. Med. 53: 2692, 1953.

#### CULDOSCOPY FOR INFERTILITY\*

An Analysis of 203 Cases

H. L. RIVA, COLONEL, MC, USA, R. P. HATCH, CAPTAIN, MC, USA, AND J. L. BREEN, CAPTAIN, MC, USA, WASHINGTON, D. C.

(From the Obstetrical-Gynecological Service, Walter Reed Army Hospital)

CULDOSCOPY as an adjunct to infertility investigations has been enthusiastically employed by this service. The purpose of this paper is to report 203 culdoscopies performed between December, 1948, and July, 1958, specifically for infertility problems. A subsequent paper will deal with the follow-up on the infertile patient, including the role of surgery as recommended mainly by the culdoscopic findings. One hundred and twenty-three of the cases presented in this report were partially analyzed in our previous report of 1,500 consecutive culdoscopies for the period ending March, 1957.

#### Historical Review

In 1946, when Albert Decker introduced culdoscopy to the literature, he stressed the value of the procedure in infertility work. Te Linde and Rutledge<sup>7</sup> in 1948, in their initial report of 56 culdoscopies, recognized the value of culdoscopy in evaluating ovarian function and the pathologic condition of the tubes. Decker<sup>3</sup> pointed out that in the presence of cornual obstruction it is impossible to determine the nature of tubal anomalies by hysterosalpingography and/or tubal insufflation. This view has also been expressed by Buxton and Southam, who feel that in cases of cornual obstruction culdoscopy may provide decisive information in evaluating patients for operation. Kelly and Rock<sup>4</sup> and Buxton and Southam<sup>2</sup> have stressed the value of culdoscopy as a complement to endometrial biopsy and endocrine surveys in patients in whom ovarian failure is suspected. Similarly, in patients with polycystic ovaries, culdoscopy serves as a convenient means for adequate visualization with minimal surgical trauma.<sup>2, 4</sup> The Stein-Leventhal syndrome may not always be suspected prior to culdoscopy.<sup>1</sup>

The largest infertility series reported is that of Kelly and Rock,<sup>4</sup> who reviewed 492 culdoscopies for infertility. Their indications for culdoscopy were: (1) failure of the usual diagnostic tests to disclose a satisfactory cause for long-standing infertility, (2) a suspicion of periadnexal adhesions based on history, pelvic examination, tubal insufflation (with delayed shoulder pain), or hysterosalpingogram with atypical dispersal of the opaque medium, and (3) ovulatory failure as suggested by temperature charts and endometrial biopsies. Their report has convincingly demonstrated that culdoscopy is of value in disclosing nonpalpable and unsuspected disease in this group of barren patients.

<sup>\*</sup>This material has been reviewed by the Office of the Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication.

y

e 7 l- e is i- y y y

n

S,

h

e

-

:

7,

y

g

### Method

The basic details of technique have been previously described.<sup>3, 5</sup> All patients are hospitalized, and all culdoscopies are performed in the operating room under sterile conditions. The use of a knee rest previously reported by this service<sup>6</sup> has permitted the performance of culdoscopies with only an anesthetist and operator present, and proper positioning is maintained under all forms of anesthesia.

Regional anesthesia (Table I) has been the method of choice. Caudal anesthesia was used during the earlier years of the study, but at present isobaric spinal anesthesia to a level of T-10 with utilization of 6 to 10 mg. of Pontocaine without an adrenergic agent has been the preferred method. Local anesthesia has been used in selected cases.

TABLE I. ANESTHESIA

	PATIENTS		
TYPE	NO.	%	
Spinal	175	86.2	
Caudal	15	7.4	
Pudendal and paracervical block	12	5.9	
Gas-oxygen-ether	1	0.5	
Total	203	100.0	

The puncture site is not routinely closed unless it has been necessary to enlarge it or if there has been bleeding from the site. In cases with cul-de-sac thickening, direct-vision enlargement of the puncture site has reduced the rate of failure. Closure is easily accomplished with the patient in the cul-doscopy position, thereby obviating the need for placing the patient in the lithotomy position, which would require additional draping.

Uterotubal methylene blue injection has been used routinely in all culdoscopies for infertility. Injection is performed with a standard 10 c.c. Luer-Lok syringe, a flexible metal tube, and one of 3 sizes of cervical cones. Adequate pressure is maintained, and no tubal ruptures have been observed with this technique. In the presence of marked obstruction, a pronounced distribution of the dye within the broad ligaments and uterus may occasionally be noted. Injection has proved especially useful in patients having equivocal hysterosalpingograms and/or Rubin tests. Several cases have been observed in which x-rays were interpreted as showing obstruction, but at the time of culdoscopy methylene blue injection demonstrated unequivocal tubal patency.

At the time of culdoscopy, and with the patient in the culdoscopy position, dilatation, curettage, cervical biopsy, and, when indicated, shallow therapeutic surgical cervical conization are performed. There is no contraindication to curettage following methylene blue injection in that the dye is removed by the solvents used in hematoxylin and cosin staining methods.

### Indications

Culdoscopy is performed on infertility patients after the usual clinical investigations have been completed. This includes routine medical history and a confidential questionnaire on both partners as well as semen analysis, baseline blood studies, urinalysis, Papanicolaou smears, cervical culture, metabolic studies when indicated, Huhner test, endometrial biopsy, Rubin test, and hysterosalpingograms. Culdoscopy is essential in patients in whom an obvious cause for infertility has not been elicited, when findings require

further evaluation, or when findings are equivocal. These indications conform closely to those of Kelly and Rock. With such broad indications, culdoscopy has virtually become a routine part of the infertility work-up.

In 43.3 per cent of the patients studied (Table II) preculdoscopy investigation yielded insufficient information for a satisfactory impression of the probable cause for infertility. Chronic pelvic inflammatory disease and endometriosis were the most common diagnoses prior to culdoscopy.

TABLE II. PRIMARY IMPRESSION

	PATIENTS		
IMPRESSION	NO.	1 %	
Infertility, cause unknown	88	43.3	
Pelvic inflammatory disease	64	31.5	
Endometriosis	23	11.3	
Adnexal mass	7	3.4	
Myomas	7	3.4	
Anomaly	5	2.5	
Stein-Leventhal syndrome	5	2.5	
Adhesions due to previous operation	4	2.0	
Total	203	100.0	

## Findings

Adhesions due to chronic pelvic inflammatory disease were found in 48.3 per cent of the series (Table III). In many of this group the pathological changes were nonpalpable and entirely unsuspected, yet severe enough to interfere with ovum transport. Similarly, much of the endometriosis found in 25.5 per cent of the patients was minimal and nonpalpable. Of the 10 cases of Stein-Leventhal syndrome, only 5 were diagnosed prior to culdoscopy.

TABLE III. FINDINGS

	PATIENTS		
FINDING	NO.	%	
Pelvic inflammatory disease	98	48.3	
Endometriosis	51	25.5	
Normal internal genitals	21	10.3	
Myomas	13	6.4	
Stein-Leventhal syndrome	10	4.9	
Adhesions due to prior operation	10	4.9	
Ovarian cysts	4	1.9	
Solid ovarian tumors	2	10	
Bicornuate uterus	1	0.5	
Hypoplasia of internal genitals	1	0.5	
Failed culdoscopy	10	4.9	

Culdoscopy failed to contribute to the infertility work-up in the 4.9 per cent of patients in whom culdoscopy failure was encountered. Negative information was obtained in 10.3 per cent in whom culdoscopy revealed grossly normal internal genitals. Such negative findings, however, are of positive value in contributing to the over-all infertility investigation.

The procedure was particularly rewarding in the group of 82 patients with completely negative studies up to the time of culdoscopy (Table IV). All of this group were felt to have normal pelves, and hysterosalpingograms were reported as normal. Only 14, however, were felt to have normal pelves after culdoscopic evaluation. Chronic pelvic inflammatory disease was found in 35.4 per cent and endometriosis in 29.3 per cent of this group.

r

1-

y e

r

TABLE IV. CULDOSCOPIC FINDINGS IN 82 CASES OF INFERTILITY WITH NO CLINICAL FINDINGS OR PREOPERATIVE DIAGNOSIS

	PATIENTS		
CULDOSCOPY DIAGNOSIS	NO.	9/0	
Pelvic inflammatory disease	29	35.4	
Endometriosis	24	29.3	
Normal internal genitals	14	17.1	
Myomas	9	11.0	
Stein-Leventhal syndrome	2	2.4	
Postoperative adhesions	1	1.2	
Hypoplasia of internal genitals	1	1.2	
Failed culdoscopy	2	2.4	
Total	82	100.0	

Interestingly, the preoperative impressions of a specific disease entity or of a normal pelvis were confirmed by culdoscopic examination in only 46.8 per cent of the series. The preculdoscopic impressions were found to be in error in 48.3 per cent of patients. These findings appear to substantiate the well-known fallibility of pelvic examination, even in the hands of specialists.

## Failure

In 10 patients it was impossible to enter the peritoneum, thus giving a failure rate of 4.9 per cent. The leading cause of failure (Table V) was cul-de-sac thickening due to adhesions from chronic pelvic inflammatory disease and endometriosis as confirmed by laparotomy on all of these patients. Perforation of the rectum occurred in two patients and culdoscopy was discontinued. Perforation of a hydrosalpinx caused the procedure to be discontinued in one patient, although the diagnosis was confirmed, drainage established, and no sequelae resulted from the perforation.

TABLE V. CAUSES OF FAILURE

Dense cul-de-sac adhesions	7
Perforation of rectum	2
Perforation of hydrosalpinx	1
Total	10 (4.9%)

## Complications and Morbidity

There were no deaths and no instances of postoperative febrile morbidity. Complications occurred in 10 patients (Table VI). Spinal headaches were noted to occur no more frequently than when this form of anesthesia was used for other procedures. The 2 rectosigmoid perforations were both extraperitoneal. These were repaired primarily and healed without sequellae. The one case of transient brachial plexus paresis occurred when the shoulder brace was approximated too closely to the neck. In this instance there was complete and rapid regression over a 2-week period. The shoulder brace should always be positioned over the acromion to obviate any possible pressure point. One patient who had a colpotomy at the time of culdoscopy was readmitted a week following discharge because of bleeding following coitus which, as the patient was told, is contraindicated within this period of time. The instance of tension pneumothorax which occurred during culdoscopy was felt by the medical and surgical thoracic consultants to be on the basis of a pre-existing and unrecognized pulmonary lesion.

TABLE VI. COMPLICATIONS

Severe spinal headache	4
Rectosigmoid perforation	2
Perforation of hydrosalpinx	1
Transient brachial plexus neuropathy	1
Colpotomy bleeding, delayed	1
Tension pneumothorax	1
Total	10 (4.9%)

## Comment

In the evaluation of the infertile woman, culdoscopy has become a valuable adjunct to other methods of investigation. Its greatest value would appear to be in disclosing minimal and nonpalpable disease which cannot be determined by means other than visualization by laparotomy. trauma is minimized and a complete evaluation of the patient is possible prior to any definitive operation. When combined with uterotubal methylene blue injection, culdoscopy has proved to be superior to the Rubin test and hysterosalpingograms. In the evaluation of adnexal conditions, it can unequivocally corroborate the interpretations made on the basis of x-ray studies. Those patients who are fearful of x-ray studies, in view of the recent emphasis upon genetic sequellae of radiation, can be adequately evaluated by culdoscopy and injection.

The rate of culdoscopy failure may be expected to be high in the infertility group of patients by virtue of the increased incidence of chronic pelvic inflammatory disease and endometriosis in this group. Complications and morbidity are minimal.

## Summary

A review of 203 patients having culdoscopies for infertility at Walter Reed Army Hospital between December, 1948, and July, 1958, has been presented. The indications, preoperative impressions, findings, and minimal complications have been discussed. The value of culdoscopy in infertility investigations has been emphasized.

#### References

- Buxton, C. L., and Herrmann, W.: Am. J. Obst. & Gynec. 68: 786, 1954.
   Buxton, C. L., and Southam, A. L.: Human Infertility, New York, 1958, Paul B. Hoeber, Inc.
   Decker, A.: Culdescopy, A. Now Tochsicus in Constant Control of Control of
- 3. Decker, A.: Culdoscopy: A New Technique A.:
  Philadelphia, 1952, W. B. Saunders Company. A New Technique in Gynecologic and Obstetric Diagnosis,
- Kelly, J. V., and Rock, J.: Am. J. Obst. & Gynec. 72: 523, 1956.
   Riva, H. L., Hatch, R. P., and Breen, J. L.: Obst. & Gynec. 12: 610, 1958.
   Riva, H. L., Staples, P. P.: Am. J. Obst. & Gynec. 76: 63, 1958.
- 7. Te Linde, R. W., and Rutledge, F.: Am. J. OBST. & GYNEC. 55: 102, 1948.

# SIGNIFICANCE OF PERFORMING DUAL SMEAR EXAMINATIONS IN A MASS SCREENING SURVEY FOR UTERINE CANCER\*

Y. S. Song, M.D., Herbert Fanger, M.D., and Thomas H. Murphy, M.D., Providence, R. I.

(From the State Cancer Cytology Laboratory, Rhode Island Hospital, Unit "K")

d

l

S

THE University of Tennessee, in conjunction with the National Cancer Institute, has recently studied, in a large population group, the incidence of cancer of the genital tract detected by exfoliative cytologic studies with confirmatory biopsy.<sup>1</sup>

Intraepithelial carcinoma of the cervix or invasive cancer was detected in 627 women of the first 95,000 examined (0.78 per cent). Almost 5 in 1,000 (0.47 per cent) of all women examined in the first screening had unsuspected disease. In an attempt to evaluate the incidence of genital tract cancer in different population groups, the National Cancer Institute is supporting similar studies in Providence, Rhode Island; Columbus, Ohio; Louisville, Kentucky; Detroit, Michigan, and a few other places throughout the country. The following is a report of the results of the first 25,000 cases examined in Rhode Island. This state has a considerably large adult female population ranging from 225,000 to 250,000 women who are over 20 years of age; 98.5 per cent of them are white, the remaining 1.5 per cent non-white.

## Materials and Methods

The routine procedures for this project consist of a vaginal fluid smear aspirated from the posterior fornix and a smear made by scraping material from the cervical os with a wooden spatula. As a rule, the routine vaginal smear taken from the posterior fornix of the vagina has great applicability to mass screening as demonstrated by the Memphis project. It is also believed that the percentage of positive findings can be increased by making additional smears with the cervical scraping method.<sup>2</sup> There are approximately 360 physicians who are participating in this project, and they were instructed to take the vaginal aspiration smear first followed by a scraping smear. All the specimens are prepared by the physicians; none of them are made by the nurses or technical personnel. Additional specimens are available from 10 clinics which were established for the project. Dual smear examinations are routinely performed on all subjects and both types of smears are screened by separate groups of people, checked by the senior checker, and rechecked by pathologists. The project has concentrated its efforts on obtaining both types of smears from asymptomatic women and has urged physicians to submit smears taken from suspected cases or from women with known carcinoma of the genital tract to

<sup>\*</sup>Presented at Sixth Annual Meeting, Inter-Society Cytology Council, New York, N. Y., Nov. 14, 1958.

hospital cytology laboratories in the state. The pathologists of Rhode Island have kindly made available the biopsy specimens for examination. Our laboratory performs step serial sections on all cone biopsies and on other selected cases. A comparison has been made of the accuracy and efficiency of both types of smears on all cases of carcinoma in situ, invasive carcinoma of the cervix, and adenocarcinoma of the fundus. Tables I and II show the results of the project.

TABLE I. CYTOLOGIC FINDINGS IN 25,000 CASES

Positive (biopsy recommended)	288	(1.1%)
Suspicious (repeat smear requested)	220	(0.8%)
Atypical	2,942	(11.0%)
Unsatisfactory	550	(2.2%)
Negative	21,000	(84.0%)

TABLE II. BIOPSY RESULTS IN 288 CASES

Carcinoma in situ of cervix	148
Squamous cell carcinoma	28
Adenocarcinoma of fundus	19
Squamous cell carcinoma of vagina	6
Carcinoma of ovary	1
Borderline lesion of cervix	23
Atypical hyperplasia of cervix	10
Biopsy inadequate	4
Biopsy negative	21
Biopsies to be performed	28
Total	288

Three pathologists independently reviewed all biopsy specimens of the cervix which were diagnosed as carcinoma in situ, borderline lesions, or atypical hyperplasia. A diagnosis of carcinoma in situ was made only if there was unanimous agreement. Borderline lesions were those cases suggestive of carcinoma in situ but lacking unanimity of diagnosis by the pathologists.

Table III compares the diagnosis made with the 2 cytologic techniques in cases proved to be carcinoma in situ by biopsy. It is evident that the cervical scraping smear detected more cases of tumor than the vaginal aspiration smear. In 45 cases only the cervical scraping smear enabled a diagnosis of cancer.

TABLE III. CYTOLOGIC READINGS

	CLASSIFICATION*					
TYPE OF CANCER	CS POSITIVE VA NEGATIVE	CS POSITIVE VA ATYPICAL	CS POSITIVE VA SUSPICIOUS	CS POSITIVE VA POSITIVE	CS NEGATIVE VA POSITIVE	TOTAL
Carcinoma in situ	30	15	26	68	9	148
Squamous cell carcinoma of cervix Adenocar-	6			19	3	28
cinoma of fundus	4			10	5	19

\*CS = cervical scraping smear method; VA = vaginal aspiration smear method.

However, in the majority of cases (94), both techniques detected cancer. In 9 cases only the vaginal aspiration smear showed abnormal cells. Table III also demonstrates in invasive squamous cell carcinoma the number of cases detected by both the cervical scraping smear and the vaginal aspiration smear. The results of the study on 19 cases of adenocarcinoma of the fundus are also shown.

Table IV shows the distribution of the age incidence of patients with carcinoma in situ in our series. The youngest patient was 22 years of age. The findings were similar to the results of the University of Tennessee. incidence of patients with squamous cell carcinoma is also shown. It should be noted that the age incidence in squamous cell carcinoma tends to be higher than that in carcinoma in situ.

TABLE IV. AGE INCIDENCE

	AGE (YEARS)							
TYPE OF CANCER	10-20	21-30	31-40	41-50	51-60	61-70	OVER 71	TOTAL
Carcinoma in situ Squamous cell carcinoma	None	17	68	36	18	9	None	148
of cervix	None	None	3	9	12	2	2	28

Ninety-two cervical cone and 56 cervical biopsy specimens were submitted in the cases of carcinoma in situ. These were examined by step serial sections; every tenth section was stained.

Despite the dual smear technique, a small number of false-negative cases occurred which seems inevitable in a mass screening survey. Six false-negatives were reported for adenocarcinoma of the fundus, 3 for squamous cell carcinoma of the cervix.

Table V demonstrates the value of the screening survey; 98.5 per cent of the smears were taken from white women and 1.5 per cent from non-white women in the state of Rhode Island. One case of carcinoma in situ was found in a Negro patient and the remaining 147 cases were found in white patients. All cases of invasive carcinoma and adenocarcinoma of the fundus were found in white women.

TABLE V. VALUE OF SCREENING SURVEY

TYPE OF CANCER	PE OF CANCER CONFIRMED CASES		NO. OF UNSUSPECTED CASE	
Carcinoma in situ of cervix	148	11	137 (92%)	
Invasive carcinoma of cervix	28	15	13 (46%)	
Adenocarcinoma of fundus	19	8	11 (55%)	

#### Summary

The dual smear examinations (vaginal aspiration and cervical scraping smears) in a screening survey for uterine cancer are considered to be highly effective in the detection of carcinoma of the cervix and adenocarcinoma of the fundus. Continued examinations of both types of smears seem justified since both specimens have a definite diagnostic value.

#### References

- Erickson, C. C., et al.: J. A. M. A. 162: 167, 1956.
   Simon, T. R., Durfee, G., and Ricci, A.: Transactions of Third Annual Meeting of the Inter-Society Cytology Council, 1955.

# A CERVICAL BIOPSY INSTRUMENT: INTRODUCTION OF A NEW TRACHELOTOME

Louis H. Averbach, M.D., Philadelphia, Pa.

(From the Department of Obstetrics and Gynecology, Frankfort Hospital)

THE PURPOSE of this paper is to introduce an inexpensive, simple, and yet quite effective cutting instrument for obtaining circular biopsies of the squamocolumnar portion of the cervix. The diagnostic and therapeutic merits of this procedure have been discussed quite adequately elsewhere<sup>1, 2</sup> and are beyond the scope of this brief article.

## Description

This trachelotome consists of a one-piece (excluding blade) cylindrical metal handle with a somewhat angulated tip to which the blade is attached. This arrangement permits easy cleaning and sterilization, economy of manufacture, and elimination of loss of small parts. In principle it is comparable to a "potato peeler" inasmuch as the thickness of the biopsy (or "peel") is governed by the space between the blade and the underlying "bar." This tends to keep the biopsy uniformly thick even when the endocervical periphery is somewhat irregular. This space can be varied in manufacturing the instrument to give whatever thickness of tissue is desired.

It was felt that a straight blade would give a more predictable cut than a curved one. For this reason a thin, sharp blade with a small hole at each end is utilized. It is held quite snugly by traction on 2 pins on the flexible "bar" of the instrument, just as the blade of a hack saw is held. The blade itself is sharp, inexpensive, and disposable. Attachment or removal of the blade is

blade

y

SIDE VIEW WITH BLADE DETACHED

TOP VIEW WITH BLADE ATTACHED

(Tip only shown)

Full Scale

Fig. 1.—A simple trachelotome. The sketch shows the one-piece construction and the method of attachment of the disposable blade. The springiness of the tlp holds the blade quite securely on the two pins.

accomplished easily by flexing the "bar" slightly. Since the blade may be inserted with the cutting edge on either side, the circular biopsies may be taken clockwise or counterclockwise.

The rather narrow tip of the instrument permits biopsy of most cervices prior to dilatation, thus avoiding traumatization of any neoplastic tissue which may be present. Furthermore, since there is no bare point on the instrument (as on a scalpel), undercutting and the accompanying increased bleeding are eliminated.

## Technique

Use of the instrument is quite simple. The cervix is exposed and prepared in the usual manner. A tenaculum is used to grasp and steady the cervix. The instrument is inserted into the endocervical canal. With the blade pressed lightly against the squamocolumnar portion of the cervix, the instrument is moved with short, sawing strokes and rotated circumferentially. A good "cold conization" specimen is thus obtained in a few moments, the collar of tissue representing the entire squamocolumnar portion of the cervix. By starting at a specific point along the cervical periphery and sectioning the tissue serially, it may be possible to localize the point of origin of any neoplastic tissue in the specimen.

Bleeding is controlled in the usual manner, e.g., with oxidized cellulose, gauze packing, cauterization, coagulation, or nothing at all.

## Summary

A simple, inexpensive, and yet effective instrument for obtaining circular biopsies of the squamocolumnar portion of the cervix is described.

I wish to express my appreciation to Mr. Aaron Kirpich, M.S., who made the first working model of this instrument.

Addendum.—Since this paper was written, we have used a completely disposable biopsy knife. This is made of plastic (except for the blade) and resembles closely the knife described above. It appears to have the same indications and advantages as the steel instrument. Furthermore, it may be manufactured and packaged in sterile form quite inexpensively and can be made available for immediate use at a moment's notice.

Since purchase of a steel knife handle is obviated, this plastic instrument seems to be more economical in institutions where only occasional cold conizations are performed.

## References

- Ayre, J. E.: J. A. M. A. 138: 11, 1948.
   Fleming, A. R.: J. A. M. A. 168: 886, 1958.

5534 LARGE STREET

# AN EVALUATION OF ROUTINE CULTURE EXAMINATIONS FOR TRICHOMONAS VAGINALIS AND CANDIDA\*

DANIEL H. CLARK, M.D., AND EDWARD SOLOMONS, M.D., BROOKLYN, N. Y.

(From the Department of Obstetrics and Gynecology, State University of New York, Downstate Medical Center, and Maimonides Hospital)

IN RECENT years much research has been carried out on Trichomonas vaginalis and Candida as causative organisms in vaginitis. Unfortunately, uniform methods of investigation have seldom been adopted, with the result that conclusions tend to vary widely. For instance, though a higher incidence of T. vaginalis has been found in pregnant patients than in nonpregnant patients, the opposite has also been claimed. Furthermore, though Candida has been shown to be more prevalent than Trichomonas in nonpregnant patients, the contrary has also been found. Therapeutic results are also confusing especially in Trichomonad infection, for which a 90 per cent cure rate was reported 30 years ago. Since then many compounds have become available for which excellent results have been claimed, yet the final consensus of gynecological opinion is that there is no acceptable treatment at the present time.

Although satisfactory methods of culture are available for both *T. vaginalis* and Candida, many investigators ignore them in favor of direct microscopic examination and initial clinical response to therapy. The culture methods are simple to interpret and the technique requires the presence of comparatively few organisms to obtain a growth. They are not dependent upon the skill and patience of the individual who examines the slide or evaluates the clinical response. Hence, they are essential in establishing uniform statistics of the incidence of *T. vaginalis* and Candida and in determining the efficacy of therapy.

The purpose of this study was:

1. To compare the accuracy of the culture method with that of the wetsmear technique for the detection of *T. vaginalis*.

2. To determine the general incidence of *T. vaginalis* and Candida in pregnant and nonpregnant women.

3. To determine the influence of age, parity, and pregnancy on the incidence of *T. vaginalis* and Candida.

#### Clinical Material and Methods

A total of 1,016 consecutive patients attending the obstetrical and gynecological clinics of Maimonides Hospital were examined for the presence of *Trichomonas vaginalis* and Candida. Of these, 739 were pregnant and 277 were

<sup>\*</sup>Presented at a meeting of the Brooklyn Gynecological Society, Jan. 21, 1959.

gynecological patients. Patients who had douched the night before examination were excluded from the study. A routine prenatal or gynecological history was taken. A sterile speculum was then inserted without the use of lubricant and the vaginal secretion was obtained by the use of 3 sterile cotton-tipped applicators. Material for  $T.\ vaginalis$  studies was obtained from the posterior vaginal fornix and for Candida studies from the lateral vaginal fornices. The following techniques were used for the examination of the material obtained for identification of  $Trichomonas\ vaginalis$ :

1. Wet Smear.—Vaginal secretions from the posterior fornix were mixed with a drop of physiological saline on a glass slide and a cover-slip was applied. The slides were examined microscopically in order to identify motile Trichomonads. The smear method was used, as it has been found to be more con-

venient and just as accurate as the hanging drop technique.4, 6, 7, 8

2. Cultures.—STS (simplified trypticase serum) medium<sup>7, 9</sup> was used with the addition of streptomycin and penicillin. More recently Kupferberg<sup>10</sup> has suggested the use of 0.1 per cent chloramphenicol, added directly to the medium before autoclaving. This medium was inoculated with the specimen and incubated within a short time at 37° C. for 48 hours. If no growth occurred, the cultures were incubated for 3 more days and re-examined. This technique has been used by others<sup>2, 8, 11-14</sup> with satisfactory results.

In the investigation of candidiasis, Nickerson's medium was used for culture. A Nickerson slant was streaked with the secretion-moistened applicator. It was then incubated at room temperature up to 3 days and examined for the presence or absence of chocolate-brown to black colonies. This method is simple and has been widely used.<sup>15–19</sup>

Patients who had positive cultures were treated with various compounds and re-examined periodically for the presence of organisms. The above-mentioned techniques were used at each examination. A total of 2,653 examinations for *T. vaginalis* and Candida were done. The therapeutic agents used will not

be discussed in this paper.

#### Results

A Comparison of the Effectiveness of Wet Smears and Cultures in Trichomoniasis.—During the course of this study 2,653 examinations for T. vaginalis were performed for the purpose of diagnosis and evaluation of therapy. Of the 319 cases positive for Trichomonas, 312 cases, or 97.8 per cent, were positive on culture while only 150 cases, or 47 per cent, were positive on smear alone. The discrepancy between the positive findings on STS culture and wet smear is also stressed by the following findings: Whereas in 169 cases the cultures were positive but the wet smears were negative, the wet smears were positive and the cultures negative in only 7 cases. These findings seem to indicate the superiority of STS culture medium for the diagnosis of Trichomonas as compared to the wet smear technique. This contention has been supported by others. For instance, in experimentally infected Rhesus monkeys, it has been found<sup>20</sup> that 31.6 per cent that were negative by intensive microscopic search were positive by the culture technique. Kean and Day<sup>2</sup> also compared the relative value of the wet smear and culture techniques. They found that T. vaginalis would not have been detected in about 30 per cent of their patients if only a wet smear examination had been made.

It was noted in this study that there was a direct relationship between the severity of infection, the number of organisms, and the frequency with which a positive smear was obtained. For instance, many patients who were clinically improved by treatment, and whose wet smear became negative, often remained

positive on culture. Kean and Day's report is based entirely on untreated patients in whom the number of organisms is relatively large, which would account for their incidence of 30 per cent missed diagnoses by smear as compared with our figure of 53 per cent.

From these observations we believe the culture method is more accurate and should therefore be used routinely in controlled investigations for the detection of *T. vaginalis*. This is difficult in private practice unless the physician has fresh medium available and is able to submit it to a laboratory for incubation and evaluation.

A Comparison of the Incidence of T. Vaginalis and Candida in Pregnant and Nonpregnant Patients.—It is generally accepted that there is an increased incidence of T. vaginalis in the vagina during pregnancy. However, in this study the reverse was found (Table I), which coincides with the work of

TABLE I. COMPARISON OF THE INCIDENCE OF T. VAGINALIS AND CANDIDA IN PREGNANT AND NONPREGNANT PATIENTS

	PREGNANT (739 PATIENTS)				ALL PATIENTS (1,016 PATIENTS)	
	NO.	%	NO.	%	NO.	%
T. Vaginalis	104	14.1	55	19.9	159	15.7
Candida	202	27.3	45	16.2	247	24.3
Both	43	5.8	8	2.9	51	5.0

others.<sup>2, 4, 11</sup> This higher incidence of Trichomonas during pregnancy was stated to be evidence that estrogens are necessary for their growth.<sup>21</sup> Kupferberg and Johnson,<sup>22</sup> however, demonstrated under experimental in vitro studies that female sex hormones have no effect upon increase in cell population of bacteria-free cultures of *T. vaginalis*. Our findings support this work.

The widely accepted belief that there is an increased incidence of Candida during pregnancy is confirmed by our investigation. Although there is a higher incidence of candidiasis than of trichomoniasis in pregnant women, the opposite is found in nonpregnant women. One study<sup>3</sup> found that the incidence of Candida was much higher than of Trichomonas in both pregnant and nonpregnant patients. However, a culture method was used (Nickerson's medium) for determining the presence of Candida, and direct microscopic examination for determining the presence of T. vaginalis. Gardner, Dampeer, and Dukes<sup>4</sup> reported an equal incidence of trichomoniasis and candidiasis in pregnant women but a routine culture examination was not used. We feel that in order to compare the occurrence of these diseases culture methods must be used in each instance.

The occurrence of simultaneous infection with both organisms is important when treatment is being considered. We found that 5 per cent of all patients examined had both infections simultaneously. However, if the patients in whom either organism was found are considered, the incidence of combined infection was 14 per cent. These figures might appear to warrant the use of medication containing a fungicide and a trichomonacide in the treatment of all cases of trichomoniasis. This contention has also been expressed in the literature.<sup>23</sup>

The Incidence of T. Vaginalis and Candida in Relation to Age.—The figures in Table II show that between the ages of 10 and 50 there is little variation in the incidence of either Trichomonas or Candida. After the age of 50, there is a decrease in the incidence of Candida, and after 60, in Trichomonas. The incidence of both infections rises in women over the age of 70; however, there are only 9 cases in this group.

Incidence of T. Vaginalis and Candida in Relationship to the Menopause.—
The incidence of T. vaginalis and Candida in postmenopausal women varies considerably in published reports. For instance, Trussell,¹ summarizing the literature, concluded that "Trichomonas is less frequent in older women," and Bernstine and Rakoff<sup>6</sup> arrived at a similar conclusion. However, others², 8, 24 found trichomonads in from 9 to 15 per cent of postmenopausal women. Similarly, a discrepancy of views exists with regard to the prevalence of candidiasis in postmenopausal women. Some¹5, 25 report a low incidence of candidiasis in these patients while others²6 maintain the incidence to be high. We found (Table III) that T. vaginalis and Candida do occur in postmenopausal women but that the incidence is less than in premenopausal women.

TABLE II. INCIDENCE OF TRICHOMONAS VAGINALIS AND CANDIDA IN RELATION TO AGE

		CAN	DIDA	TRICHO	OMONAS	TRICHO AND CA	
AGE (YEARS)	TOTAL NO.	NO.	%	NO.	%	NO.	%
Pregnant Patients	.—						
10-19	108	29	26.8	12	11.1	5	4.6
20-29	430	115	26.7	60	13.9	25	5.8
30-39	179	53	29.6	31	17.3	12	6.7
40-49	22	5	22.7	1	4.5	1	4.5
50-59	0	0		0	_	0	-
Nonpregnant Pati	ents.—						
10-19	5	1	20.0	1	20.0	0	_
20-29	60	11	18.3	15	25.0	3	5.0
30-39	75	11	14.7	17	22.6	2	2.7
40-49	66	13	19.7	14	21.2	1	1.5
50-59	28	3	10.7	5	17.9	1	3.6
60-69	34	3	8.8	2	5.9	1	2.9
70+	9	3	33.3	1	11.1	0	-
All Patients							
10-19	113	30	26.6	13	11.5	5	4.5
20-29	490	126	25.7	75	15.3	28	5.7
30-39	254	64	25.2	48	18.9	14	5.5
40-49	88	18	20.4	15	17.1	2	2.3
50-59	28	3	10.7	5	17.9	1	3.6
60-69	34	3	8.8	2	5.9	1	2.9
70+	9	3	33.3	1	11.1	0	-

TABLE III. INCIDENCE OF TRICHOMONAS VAGINALIS AND CANDIDA IN RELATIONSHIP TO MENOPAUSE

	TOTAL NO.	TOTAL CANDIDA		TRICHOMONAS		TRICHOMONAS AND CANDIDA	
		NO.	1 %	NO.	0/0	NO.	%
Postmenopausal patients Premenopausal nonpreg-	78	10	12.8	9	11.5	4	5.1
nant patients	199	35	17.6	46	23.2	4	2.0

The Relationship of the Incidence of T. Vaginalis and Candida to Parity.—
There is little in the literature concerning the influence of parity on the incidence of T. vaginalis. We found a high incidence of T. vaginalis in pregnant women with one child as compared with primigravidas and multigravidas. This difference is statistically significant. We have no explanation for this high incidence and have been unable to find any reference to it in the literature.

Similarly, there is little in the literature concerning the relationship of candidiasis to parity. Our study shows no statistically significant difference in the incidence of Candida in relation to parity (Table IV). A previous study<sup>26</sup>

stated that "monilia" infection was more common in nulliparous women, but in pregnant women the infection was more common in the multigravida than in the primigravida. However, no other support for these results could be found.

TABLE IV. RELATIONSHIP OF THE INCIDENCE OF TRICHOMONAS AND CANDIDA TO PARITY

	NO. OF	TRICH	OMONAS	CAN	DIDA	TRICHO AND CA	
PARITY	PATIENTS	NO.	1 %	NO.	1 %	NO.	%
Pregnant Patient	9,—						
P0	216	24	11.1	59	27.3	9	4.2
P1	201	44	21.9	48	23.9	16	8.0
P2+	320	34	10.6	94	29.4	17	5.3
Nonpregnant Pat	ients.—						
PO	37	8	21.6	8	21.6	2	5.4
P1	52	13	25.0	7	13.5	1	1.9
P2+	185	34	18.4	30	16.2	5	2.7

Signs and Symptoms Associated with T. Vaginalis and Candida.—The incidence of signs and symptoms in patients with Candida and Trichomonas is presented in Table V. Discharge was found to be more common than pruritus in both Trichomonas and Candida infection. Other studies<sup>3, 15</sup> stated that in Candida infections pruritus was more common than discharge. There are many patients who do not have vaginal discharge but have trichomonads in the vagina. The reported incidence of this condition varies widely.<sup>24, 27</sup> Our incidence of patients with Trichomonas but without discharge was 43.1 per cent.

TABLE V. SIGNS AND SYMPTOMS ASSOCIATED WITH TRICHOMONAS VAGINALIS AND CANDIDA

	SYMPTOMS					DISCHARGE		NO SIGNS OR	
CULTURE	NO. OF	DISCH	IARGE	PRUF	RITUS	ON PH	YSICAL	SYMP	TOMS
RESULTS	PATIENTS	NO.	1 %	NO.	90	NO.	1 %	NO.	1 %
Trichomonas	160	91	56.9	65	40.7	115	71.8	41	25.6
Candida	251	130	51.8	91	36.2	157	62.7	74	29.4
Simultaneous	52	34	65.4	25	48.1	39	75.0	10	19.5
Negative	661	143	21.6	44	6.6	127	19.2	448	68.0

Many women have Candida in the vagina, but do not suffer from discharge. The incidence of this type of infection is reported as 48 per cent.<sup>16</sup> and as 62 per cent.<sup>28</sup> Our incidence is 48.2 per cent.

#### Summary

- 1. A total of 1,016 women have been examined for *Trichomonas vaginalis* and Candida. These patients were attending the prenatal and gynecological clinic.
- 2. The incidence of T. vaginalis and Candida in these patients was determined.
- 3. The incidence of T. vaginalis and Candida in relation to pregnancy, age, menopause, and parity is discussed.
  - 4. An evaluation of the signs and symptoms of these infections is presented.
- 5. In the detection of T. vaginalis the culture technique is shown to be much more accurate than the wet smear method.

We are indebted to Ortho Pharmaceutical Corporation for a grant-in-aid and for providing us with the culture media. We also would like to thank our technician, Miss Nechama Singer, for her valuable assistance in this study.

## References

- 1. Trussell, R. E.: Trichomonas Vaginalis and Trichomoniasis, Springfield, Ill., 1947, Charles C Thomas, Publisher. 2. Kean, B. H., and Day, E.:
- AM. J. OBST. & GYNEC. 68: 1510, 1954.
- Kean, B. H., and Day, E.: Am. J. Obst. & Gynec. 68: 1510, 1954.
   Pace, H. B., and Schantz, S. I.: Monographs on Therapy, New Brunswick, N. J., 1957, The Squibb Institute, vol. 2, p. 29.
   Gardner, H. L., Dampeer, T. K., and Dukes, C. D.: Am. J. Obst. & Gynec. 73: 1080, 1957.
   Greenhill, J. P.: Am. J. Obst. & Gynec. 16: 870, 1928.
   Bernstine, J. B., and Rakoff, A. E.: Vaginal Infections, Infestations and Discharges, New York, 1953, Blakiston Company.
   Kupferberg, A. B.: Internat. Rec. Med. & G. P. Clin. 168: 709, 1955.
   Buxton, C. L., and Weinman, D.: In Meigs, J. V., and Sturgis, S. M., editors: Progress in Gynecology, New York, 1957, Grune & Stratton, Inc., vol. III.
   Kupferberg, A. B., Johnson, G., and Sprince, H.: Proc. Soc. Exper. Biol. & Med. 67: 304, 1948.
   Kupferberg, A. B.: Personal communication

- 10. Kupferberg, A. B.: Personal communication.
  11. Plentl, A. A., Gray, M. J., Neslen, E. D., and Dalali, S. J.: Am. J. Obst. & Gynec. 71: 116, 1956.
- 12. Feo, L. G.: AM. J. OBST. & GYNEC. 75: 322, 1958.

- 12. Feo, L. G.: AM. J. OBST. & GYNEC. 75: 322, 1958.

  13. Hunter, C. A., Jr., and Long, K. R.: AM. J. OBST. & GYNEC. 75: 865, 1958.

  14. Wilkinson, B. M., and Williams, G. C. J.: Brit. M. J. 2: 210, 1958.

  15. Perl, G., Guttmacher, A. F., and Jakubowicz, H.: Obst. & Gynec. 5: 640, 1955.

  16. Jackson, J. L.: AM. J. OBST. & GYNEC. 72: 648, 1956.

  17. Pace, H. R., and Schantz, S. I.: J. A. M. A. 162: 268, 1956.

  18. Hengerer, A. D., and Covert, S. V.: GP 13: 88, 1956.

  19. Pickhardt, W. L., and Breen, J. L.: AM. J. OBST. & GYNEC. 74: 42, 1957.

  20. Williams, M. H.: AM. J. OBST. & GYNEC. 60: 224, 1950.

  21. Stein, I. F., and Cope, E. J. AM. J. OBST. & GYNEC. 65: 210, 1022.

- Pickhardt, W. L., and Breen, J. L.: Am. J. OBST. & GYNEC. 74: 42, 1957.
   Williams, M. H.: Am. J. OBST. & GYNEC. 60: 224, 1950.
   Stein, I. F., and Cope, E. J.: Am. J. OBST. & GYNEC. 25: 819, 1933.
   Kupferberg, A. B., and Johnson, G.: Proc. Soc. Exper. Biol. & Med. 48: 516, 1941.
   Karnaky, K. J.: Am. J. OBST. & GYNEC. 69: 225, 1955.
   Feo, L. G.: Am. J. OBST. & GYNEC. 72: 1335, 1956.
   Hesseltine, H. C.: Am. J. OBST. & GYNEC. 34: 855, 1937.
   Plass, E. D., Hesseltine, H. C., and Borts, I. H.: Am. J. OBST. & GYNEC. 21: 320, 1931.
   Peterson, P.: Am. J. OBST. & GYNEC. 35: 1004, 1938.
   Campbell R. M. and Parrett, M. H.: Am. J. OBST. & GYNEC. 59: 1005, 1950.
- 28. Campbell, R. M., and Parrott, M. H.: Am. J. OBST. & GYNEC. 59: 1005, 1950.

# A NEW AGENT FOR THE TREATMENT OF VAGINAL CANDIDIASIS

BERNARD LAPAN, M.D., NEW YORK, N. Y.

(From the Department of Obstetrics and Gynecology, Lebanon Hospital)

Variable Additional Additional Although the administration of these antibiotics to a patient may precede the development of vaginal candidiasis, the majority of women seen with this condition give no history of such antecedent therapy. We must assume that the spores of Candida albicans are more abundant and more widely disseminated than ever before. Generalized and fatal candidiasis is now being seen in its severest form of infection.

Although pregnancy, diabetes, and previous antibiotic therapy are specific predisposing factors in the etiology of vaginal candidiasis, the presence of a fungus infection must be suspected in every woman complaining of vaginal irritation, pruritus, or discharge. The classical appearance on examination of a white, caseous or flaky, sour-smelling discharge need not necessarily

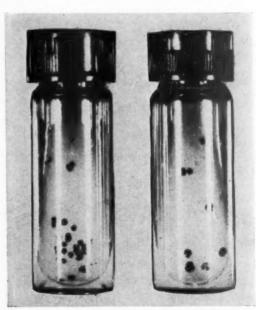


Fig. 1.-Characteristic positive Candida cultures on Nickerson's medium.

f

be present. Many of these patients present a thin, watery, sometimes brownish, discharge which appears to arise in an acutely congested vaginal mucosa. Although frequently described in the literature, the use of fresh, wet, alkaline treated, or stained smears of vaginal secretions for the diagnosis of candidiasis by identification of mycelia or spores has not been found to be of sufficient diagnostic value. The culture of the vaginal secretions on Nickerson's medium,<sup>2, 3</sup> however, produces characteristic brown or black colonies after incubation for 2 or 3 days at room temperature (Fig. 1). This is a very simple, inexpensive, and accurate office diagnostic procedure.

The numerous agents which have been used in the treatment of vaginal candidiasis include gentian violet, silver picrate, acetic acid, propionic acid, various proprietary arsenical compounds, nifuroxime, phenylmercuric acetate, and nystatin. The drug chlordantoin described in this paper represents a very effective and acceptable addition to this armamentarium.

## Materials and Methods

The chemical used in this study is 3-trichloromethylthio-5-(1-ethyl) amyl hydantoin, with the generic name chlordantoin, and the following structure:

During the course of this study, this compound has been termed E34-25.\* It has excellent activity in vitro against all of the pathogenic fungi, yeasts, and actinomycetes tested.<sup>4</sup> It shows a low level of acute and chronic toxicity in rats. In dermatologic fungus infections, it has a high degree of efficacy,<sup>5</sup> and its acceptability is enhanced by its lack of staining.

This material, chlordantoin, was initially used with excellent therapeutic effect in the form of vaginal insert tablets, each containing 100 mg. of the active substance in a 2 Gm. lactose base. The chlordantoin (E34-25) was also incorporated in a cream base. This cream was in a 1 per cent concentration, and each applicatorful contained 50 mg. of the active ingredient. The majority of patients in this study were treated with this cream formulation.

Only women with positive vaginal cultures on Nickerson's medium were included in this study. Thirty-one such patients were observed and treated. They were instructed in the vaginal insertion of either the tablets or 5 c.c. of the cream, by means of disposable plunger applicators, twice daily for a period of 14 days. One week after the completion of treatment a repeat culture was taken. If the culture remained positive, a repeat course of treatment was given.

During the acute phase of the infection, coitus was prohibited. No douches were permitted and the patients were instructed not to use soap in the region of the vulva.

<sup>\*</sup>Sporostacin Chlordantoin Vaginal Cream, Ortho Pharmaceutical Corporation, Raritan, N. J.

### Results

Of the 31 patients treated, all reported relief of the symptoms of vaginal discomfort within 2 days. Many stated that improvement began within a few hours after the first vaginal application of the drug. The associated intertrigo seen in some cases also disappeared rapidly. The Nickerson's cultures remained positive, however, and this required a second course of treatment in 15 of the 31 cases. After the 2 courses of treatment, all patients were normal except 2 and these women were given third courses of treatment with chlordantoin. One then became culture negative, but the last of these patients, who had a well-advanced pregnancy, was persistently culture positive on Nickerson's medium even after the fourth course although her signs and symptoms had long since been controlled. The results are summarized in Table I.

TABLE I. SUMMARY OF RESULTS OF TREATMENT OF VAGINAL CANDIDIASIS WITH CHLORDANTOIN VAGINAL CREAM

Negative cultures at conclusion of therapy Positive cultures at conclusion of therapy	. 30
Total	31
1 course of treatment required in	16 patients
2 courses of treatment required in	13 patients
3 or more courses required in	2 patients
Total	31

The side effects noted were minimal. A few patients complained of a slight stinging or burning sensation immediately after application of the medication during the acute phase. There were no complaints, such as excess moisture or oozing, referable to the physical properties of the cream. The use of the medication was continued during the menstrual flow in most cases, with no objection from the patients. The lack of color and absence of objectionable odor, as well as the consistency of the cream appeared to contribute to the high degree of patient acceptance of this medication and of cooperation throughout treatment.

#### Comment

The use of this new compound, chlordantoin, in the treatment of vaginal candidiasis offers the advantages of simplicity, patient acceptance, and rapid relief of symptoms, together with a high percentage of culture-free cures. Its use should, however, be controlled by the culture of vaginal secretions on Nickerson's medium, both for the initial diagnosis and for termination of therapy. Whenever possible, this drug should be continued until the cultures are negative. Some patients wanted to discontinue the use of the medication as soon as their symptoms were relieved, and it was necessary to insist that therapy should be extended until the causative organism was no longer present on culture.

Although other substances are available for the treatment of vaginal candidiasis, this compound will take its place with them as one of the most rapidly effective and dependable of all. Its use should also find acceptance in the prophylaxis of vaginal candidiasis in women receiving broad-spectrum

antibiotic therapy, as well as in the prevention of neonatal Candida infections. It has been found that about 20 to 30 per cent of pregnant women at term harbor Candida in the vagina.6, 7 The routine use of Nickerson's cultures and appropriate antifungal therapy should be considered in all women with vaginal discharge who are approaching term.

## Summary

A new antimonilial agent, 3-trichloromethylthio-5-(1-ethyl) amyl hydantoin, has been tested in 31 cases of yeast vaginitis. A single course rendered 16 of these negative as judged by culture on Nickerson's medium. Of the 15 patients who required re-treatment, 13 achieved negative cultures from the second course. The medication appears to be an effective treatment for vaginal candidiasis.

#### References

- 1. Eschwege, J.: A. M. A. Arch. Neurol, & Psychiat. 79: 250, 1958.

- Eschwege, J.; A. M. A. Arch. Neurol, & Psychiat. 79: 250, 19
   Lang, W. R.; Obst. & Gynec. Surv. 10: 546, 1955.
   Wilson, D. G.; West. J. Surg. 64: 180, 1956.
   Kupferberg, A. B., and Doscher, G. E.; To be published.
   Glick, H. V.; To be published.
   Bret, J., and Coupe, C.; J. A. M. A. 168: 458, 1958.
   Stough, W. V., and Blank, H.; Obst. & Gynec. 12: 338, 1958.

a d

S

e

## A STUDY OF THE INJECTION OF BLOOD INTRAPERITONEALLY INTO WOMEN

Observation of 28 Patients

WILLIAM C. KEETTEL, M.D., KENNETH L. KINGSBURY, M.D., AND ROBERT C. HARDIN, M.D., IOWA CITY, IOWA

(From the Departments of Obstetrics and Gynecology and Internal Medicine, State University of Iowa and the University Hospitals)

T IS often assumed that the signs and symptoms of a ruptured ectopic pregnancy are produced entirely by intraperitoneal bleeding. Although this is undoubtedly an important factor, distention and rupture of the tube, development of a hematocele, and adherence of omentum or loops of bowel also are important contributing factors. A study of the results of introduction of blood into the peritoneal cavity through the cul-de-sac was undertaken because such observations have been made rarely. In its course an opportunity arose to see whether intact red blood cells might enter the peripheral circulation in significant numbers from the abdominal cavity.

## Subjects and Procedures of Injection

Twenty-eight patients awaiting elective surgery in the Department of Gynecology were used in this study. They were thin and had relatively normal pelvic viscera. Most had been admitted for sterilization, treatment of severe functional uterine bleeding, or of carcinoma in situ. Various mixtures of blood and electrolyte solutions were injected into the peritoneal cavities. Eighteen received freshly drawn blood in A.C.D. preservative solution in amounts ranging up to 650 ml. Four received 500 ml. of blood unmodified by the addition of any diluent or anticoagulant. Five received 0.9 per cent sodium chloride in water in amounts varying from 500 to 1,800 ml. One patient was given 1,500 ml. of normal saline solution to which had been added 100 ml. of 3.2 per cent sodium citrate solution. The length of time required for administration varied from 4 to 24 minutes.

The injections were made through the posterior cul-de-sac. A cleansing enema was given in the evening and the following morning the patient's bladder was emptied. The vagina was prepared by sponging with aqueous Zephiran solution. A retractor was used to expose the cervix which was grasped with a single-toothed tenaculum. The cervix was pulled upward and the retractor was depressed posteriorly exposing the peritoneal reflection. A 13 gauge needle was introduced into the cul-de-sac. In the first few trials the vaginal mucosa was infiltrated with a 1 per cent solution of procaine but this proved as painful as the introduction of the needle without anesthesia. When the needle was in place the blood or other fluid was injected into the peritoneal

cavity (Fig. 1).

### Clinical Observations

#### Methods .-

Leukocyte counts were taken and the erythrocyte sedimentation rate was measured by the Westergren technique before injection. Blood pressure, heart rate, and body temperature were determined also. The subjects were carefully observed after injection. Their symptoms were noted and the results of palpation of the abdomen and bimanual examination of the pelvis were recorded. Changes of blood pressure and heart rate were followed until stabilization occurred and body temperature was measured rectally every 4 hours. Leukocyte counts were done at 4, 8, 12, 24, 36, and 48 hours after injection and the erythrocyte sedimentation rate was determined daily for 4 days. At first it was measured also at 5 and 8 hours after injection but this was discontinued later in the experiment. In many cases the upper abdomen was examined by x-ray. Laparotomy for the indicated procedure was performed from 1 to 8 days after injection and the viscera were carefully examined. Cultures were obtained from the peritoneal cavity and biopsies of the peritoneum were taken from the cul-de-sac.

#### Results .-

The subjects who received blood in A.C.D. solution had symptoms in from 3 to 9 minutes. Usually these were mild cramps in the lower abdomen. Several complained of rectal pain and a few had a sensation similar to menstrual Within 10 to 30 minutes some of the patients had fullness in the

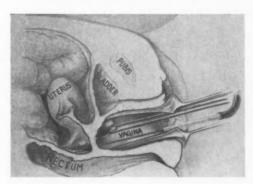


Fig. 1.-Method of injection of fluids by cul-de-sac puncture.

upper abdomen with shortness of breath and belching which often was accompanied by shoulder pain. Considerable variation was noted not only in the character of the symptoms but in their severity. Within one to 3 hours the majority of patients were free of pain, could eat, and were walking about without discomfort. The results of physical examination also varied. Soon after the injection many of the patients had slight tenderness, particularly on deep palpation. About half had rebound tenderness and a third had spasm of abdominal muscles. Movement of the uterus on bimanual examination did not produce pain. Aspirin was required for the relief of the mild symptoms in about half the patients and in one case codeine was necessary.

The four patients who received unmodified blood had minimal reactions. All complained of mild cramps in the lower abdomen lasting about 10 minutes. None had subsequent discomfort. No abnormality was noted on bimanual examination and movement of the uterus produced no pain. Two had some tenderness to deep pressure in the lower abdomen but no muscle spasm or

rebound tenderness was elicited.

Similarly, few symptoms followed the injection of 0.9 per cent NaCl solution. Most of the patients had only a slightly uncomfortable sensation of abdominal distention. The one patient who received a mixture of sodium citrate and sodium chloride solution had symptoms strikingly similar to those of the ones who were given blood in A.C.D. preservative mixture.

Thirteen of the entire group of patients had slightly elevated blood pressures at the beginning of the injection compared to measurements taken during the previous day. The blood pressure returned to normal in all subjects shortly after the injection was completed. There were also initial elevations of heart rate with a quick return to normal. Both were attributed to emotional tension. Nine subjects had an elevation of rectal temperature above 100.4° F. The highest temperature recorded was 102° F.

Leukocyte counts after injection showed significant elevations. The maximal increase occurred in the 4 to 6 hour interval. Thirty-seven per cent of the patients had elevations between 5,000 and 10,000 above the control level and in 8 per cent the increase exceeded 20,000. The highest recorded count was 31,000 per cubic millimeter. Even after normal saline solution alone was administered, rather high white-cell counts were encountered.

No change in the erythrocyte sedimentation rate occurred in the first 24 hours. Seventeen of the patients (69 per cent) had sedimentation rates of 50 to 60 mm, per hour on the third and fourth days. These were not related to the type or the amount of fluid injected.

Because some patients complained of shoulder pain, upper abdominal roentgenograms were made in 12 subjects. Seven had free air beneath the diaphragm. This occurred despite every precaution and undoubtedly contributed to the shoulder pain.

Laparotomy for the indicated procedure was done from one to 8 days after injection. When saline solution alone had been administered no peritoneal reaction was found. When blood in A.C.D. solution had been used a variety of reactions was present. Most commonly the unopened peritoneum appeared faintly blue. The bowel, omentum, and pelvic viscera were coated with a very thin layer of blood. Usually a few small clots or a small amount of hemolyzed blood was present in the cul-de-sac. In only 3 patients was there evidence of tissue reaction on inspection. The injection of unmodified blood produced a very different picture. The peritoneum was not discolored nor were the viscera coated. From 100 to 300 ml. of clotted blood was in the cul-de-sac. One patient had adhesions of the Fallopian tubes, sigmoid colon, and broad ligaments with considerable edema. In the rest there was only minimal edema.

TABLE I. PERITONEAL CULTURES

TYPE OF BACTERIA*	NO. OF CASES
From 23 Patients Injected (Bacteria Recovered in 3.	5%).—
Staphylococcus	11
Streptococcus, nonhemolytic	1
Streptococcus, alpha hemolytic	1
Alcaligenes faecalis	1
Micrococcus	1
Diphtheroid	4
From 28 Patients Not Injected (Bacteria Recovered i	n 45%).—
Staphylococcus	9
Diphtheroids	4

\*Two or more types were often present.

Examination of the peritoneal biopsies showed a thin layer of loose connective tissue as the basic structure. There was moderate infiltration by chronic inflammatory cells which was most marked around blood vessels and,

uof

m se Srts ns 0ve. iof el nt as 4 0

ıl e

ia n d t e d

in some instances, involved the vessel walls. Although most of the inflammatory cells were lymphocytes, a few polymorphonuclear leukocytes were present. In addition, there were foci of extravasated erythrocytes and areas of pig-

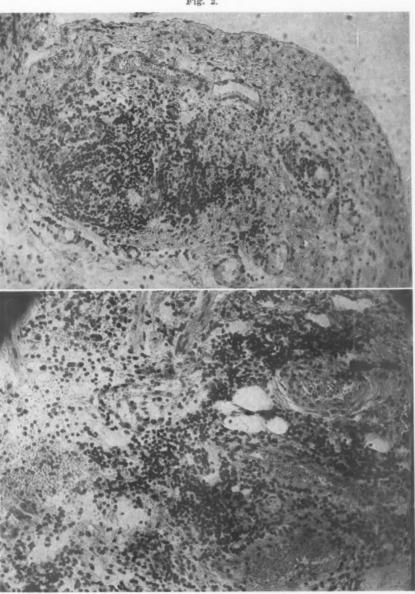


Fig. 2.—Low-power view of peritoneal biopsy showing infiltration with chronic inflammatory cells.

Fig. 3.—High-power view of peritoneal biopsy showing inflammatory cells and the cellulitis involving the vessel walls.

ment deposition (Figs. 2 and 3). These findings were interpreted as representing extensive chronic and subacute vasculitis and perivasculitis rather than operative trauma.

Cultures taken from the peritoneal cavity at operation (Table I) showed bacteria to be present in 35 per cent of the cases although no clinically apparent infections were encountered. To check this observation, similar cultures were obtained from 28 other patients who had no obvious infection and who had not been subjected to intraperitoneal injection. Bacteria of the same types as those found in the injected patients were recovered in 45 per cent. One may speculate whether this resulted from air-borne contamination of the open abdom in or contamination from bacteria on the skin.

## Observations on the Fate of the Injected Blood

Methods .-

Blood injected into the peritoneal cavity must be compatible to prevent untoward reaction or isosensitization. This fact made possible observations which might answer the question of whether intact erythrocytes gain entrance from the peritoneal cavity to the peripheral blood in significant numbers. The 18 patients who received from 115 to 650 ml. of blood and A.C.D. solution mixture and the 4 who received unmodified blood were used to make these observations.

The blood to be used was thoroughly mixed and an aliquot taken except when unmodified blood was employed. The erythrocytes were enumerated with the use of standard diluting pipettes and counting chambers. The concentration of hemoglobin in the mixture was measured. Finally, the concentration of free hemoglobin in the plasma was determined. All measurements were made in duplicate and the average value was calculated.

Preliminary determinations of the erythrocyte count, the hemoglobin, and the level of plasma free hemoglobin were made for each patient before injection. All subjects were tested for ABO group and their Rh types determined. In addition, their MN blood types were determined. When applicable, the blood used for injection was chosen from that group and type which made possible the identification of cells which gained access to the peripheral circulation. For this purpose the modified Ashby technique of DeGowin, Sheets, and Hamilton was used. All blood injected was compatible in so far as the ABO system was concerned with that of the patient and all were identical with that of the patient in Rh type. In 14 it was possible to administer cells which were serologically identifiable. Thus in 8 instances subjects possessing group A, Rh-positive blood were given cells which were group O, Rh positive. Two patients whose blood was group B, Rh positive received group O, Rhpositive cells. Group O, Rh-negative blood was injected into one patient who was group A, Rh negative. Two other patients who were group O, Rh positive and group O, Rh negative, respectively, and both of whom were M positive received blood of identical group and Rh type but which was N positive, M negative. With the use of proper sera, counts of inagglutinable cells were made on each patient before the administration of blood and 24 and 48 hours afterward. At the same time, the erythrocyte counts and hemoglobin concentrations of the peripheral blood were determined.

Other pertinent observations were made. Before injection of the blood and at 24 and 48 hours after administration, measurement of the levels of urea nitrogen, plasma bilirubin, and free hemoglobin in plasma in the peripheral blood of the subjects was made. Numerous determinations were done at 4, 6, 8, and 12 hours. Urine samples collected in the 12 hours after injection of the blood, in the second 12 hours, and in the next 24 hours were kept separately. Qualitative tests for bilirubin, hemoglobin, and urobilinogen were performed.

At the time of laparotomy the blood remaining in the peritoneal cavity was collected by suction into a bottle containing a measured amount of A.C.D.

solution. Aliquots of this mixture were analyzed for content of free hemoglobin, total hemoglobin, and bilirubin. The erythrocyte count was also determined. These results could be corrected for dilution and the total amounts recovered from the peritoneal cavity calculated.

### Results .-

d o-

es

d

t.

t s e e

til -- s

. .

The initial inagglutinable counts and the increments at 24 and 48 hours are given in Table II. Increases in the counts at 24 hours ranged between 200 and 29,000 inagglutinable cells per cubic millimeter of peripheral blood. The mean increase was 10,800. At 48 hours the increases ranged from minus 2,000 to 53,000 with a mean of 22,880.

TABLE II. INCREASE IN INAGGLUTINABLE COUNTS

CASE NO.	ML. OF BLOOD GIVEN	BLANK	INCREMENT AT 24 HOURS	INCREMENT AT 48 HOURS	CHANGE 24-48 HOURS
1*	115	10,750	800	550	-250
2	235	19,000	4.000	4.000	0
3	240	17,800	23,200	27,200	4,000
4	240	3,100	18,700	31,700	13,000
5	570	2,600	200	0	-200
7	650	18,700	13,500	21,300	7,800
8	520	21,500	18,500	53,300	34,800
9	582	100,000	5,000	12,000	7,000
10	444	6,000		42,000	
12	565	7,000	29,000	47,500	18,500
13	550	50,000	7,000	-2,000	-9,000
14	587	6,000	3,500	35,000	31,500
U4†	500	17,000	7,000	15,000	8,000
		MEAN	10,800	22,880	9,160

\*Cases 1 through 14 received blood and A.C.D. mixture.

†Case U4 received unmodified blood.

TABLE III. PLASMA FREE HEMOGLOBIN (MG. PER 100 ML.)

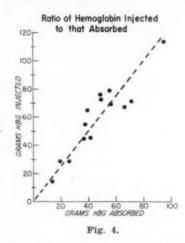
CASE NO.	ML. OF BLOOD GIVEN	CONTROL	24 HOURS	48 HOURS
1*	115	3.2	16.0	19.4
2	235	2.5	3.2	3.8
4	240	2.5	4.8	4.5
5	570	5.2	38.9	6.5
7	650	3.8	20.7	11.2
9	582	3.8	14.0	28.1
11	585	6.0	12.9	18.0
12	565	3.2	10.5	10.5
13	550	1.7	6.5	11.9
14	587	2.5	14.6	21.4
15	540	4.5	6 0	7.0
16	575	4.5	16.0	-
17	625	3.2	6.0	-
18	610	6.0	14.0	
U1†	500	3.2	7.0	13.3
U2	500	3.8	6.0	18.0
U4	500	3.5	6.0	9.1

\*Cases 1 through 18 received blood and A.C.D. mixture.

†Cases U1, U2, and U4 received unmodified blood.

Since it was evident that no large number of cells had reached the peripheral blood in 48 hours, other observations were made to find what had happened to the blood. The most interesting of the observed changes was an increase in the free plasma hemoglobin. In 17 patients who received either blood in A.C.D. solution or unmodified blood, control levels of free plasma hemoglobin were below 6.0 mg. per 100 ml. Elevations were observed in all

but 2 patients at 24 or 48 hours or both. In these 2 instances less than 250 ml. of blood had been injected. The mean elevation at 24 hours was 12.1 mg. per 100 ml. and at 48 hours it was 13.2 mg. There was no consistent pattern but much individual variation. No elevations of free plasma hemoglobin were seen before 12 hours. In some patients high levels persisted for as long as 72 hours and in others clearing of the plasma occurred between 24 and 48 hours after injection. The control values for free plasma hemoglobin and those at 24 and 48 hours are shown in Table III. Determinations of the serum bilirubin levels were made in 22 patients at 24 and 48 hours after injection of blood as well as initial determinations before injection. The control readings were all in the normal range except one. In this patient the initial level was 1.08 mg. per 100 ml. At 24 hours the value for bilirubin was 4.16 mg. per 100 ml. and at 48 hours it was 2.47 mg. Slight elevations over the control readings were consistently noted in the other 21 patients at either 24 or 48 hours.



The highest observed value was 1.35 mg. per 100 ml. Increases in the serum bilirubin above the control levels ranged from 0 to 0.70 mg. at 24 hours and from 0 to 0.74 mg. at 48 hours. There were elevations in all patients who received more than 400 ml. of blood and the greatest changes were seen in those whose free plasma hemoglobin exceeded 10.0 mg. per 100 ml. at 24 hours.

The level of blood urea nitrogen in the peripheral blood was determined before injection and at 24 and 48 hours. No significant elevations were observed.

The urine samples contained no bilirubin or abnormal amounts of urobilinogen. Three patients had hemoglobinuria of slight degree. In 2 this occurred in the first 24 hours and in one during the second day. All had elevated levels of free plasma hemoglobin although none was above 22 mg. per 100 ml. when measured.

The blood recovered from the peritoneal cavity ranged in amount from none to 180 ml. Examination by erythrocyte count and total hemoglobin estimation showed marked concentration of the magnitude of four or five times. Furthermore, there was considerable hemolysis with one-tenth to two-thirds of the hemoglobin in the peritoneal cavity in the free state. The maximal amount of free hemoglobin found was 10.0 Gm. at 6 days. Most of the hemoglobin injected as erythrocytes had disappeared, however, this ranged from 50 to 100 per cent or from 13.7 to 94.4 Gm. The total amount absorbed was directly proportional to the amount injected without regard to the time elapsed from injection to laparotomy and recovery. This relationship is

ıl.

er

at

re

12

rs

at

i-

f

S

0

shown in Fig. 4. The rate at which absorption occurred was less a function of time than an individual variation. In 10 patients who received 500 ml. or more of blood and A.C.D. solution, the amount of injected hemoglobin absorbed ranged from 42 to 100 per cent. That this was independent of time is indicated by the observation that the patient who had absorbed all the blood did so in 2 days. The one who had absorbed only 42 per cent had the laparotomy 6 days after injection. Another patient had absorbed 99 per cent at 7 days. The other 8 individuals absorbed from 60 to 90 per cent in from 3 to 8 days. There was no apparent constant time relationship to the rate of disappearance of blood from the peritoneal cavity.

#### Comment

Hemorrhage into the peritoneal cavity may be produced by a variety of pathological conditions. In gynecology the most common are ectopic pregnancy and ruptured follicle. Many clinicians have assumed that the free blood in the abdomen causes most of the symptoms and physical changes encountered. A study employing the intraperitoneal injection of blood is difficult to assess because evaluation depends on more or less indefinite clinical observations as well as the response of the patient to pain. Cole and Montgomery<sup>2</sup> have reported on 237 intraperitoneal transfusions in 117 pediatric patients. They encountered symptoms consisting of restlessness and abdominal discomfort in only 7 per cent. There were no fevers. They were most impressed by the relative freedom from symptoms. Mengert, Cobb, and Brown<sup>3</sup> have injected blood experimentally into the peritoneal cavities of women. They used blood taken from the patient and injected it unmodified through a 16 gauge needle inserted just below the umbilicus. Their findings were different from ours in They noted moderate to severe pain for a short time with some respects. tenderness elicited by deep palpation. When operation was performed in the next 24 hours about four-fifths of the blood remained liquid in the abdominal cavity and clotting was minimal. When whole blood was injected into the cul-de-sac, we noted very mild symptoms and few physical changes. At operation 48 hours later about one-half of the total quantity of injected blood remained as clots. When citrated blood was used, our observations on examination and the symptoms of the patients were quite similar to those of Mengert and his associates,3 although we recovered less blood after the longer interval. This difference in observations may be related to the site of injection. When unmodified blood is injected into the cul-de-sac it clots in a short time and the bowel, peritoneum, and diaphragm are not coated. Cramps, belching, and fullness are not encountered. With injections of citrated blood no clotting occurs. In a short time the bowel and other structures are covered by a thin film. This is followed by the symptoms described. Similarly, in acute ectopic pregnancy characterized by profuse bleeding, the blood remains liquid and many symptoms are present. In the chronic form of ectopic pregnancy or in tubal abortion characterized by minimal bleeding, however, most of the blood clots in the cul-de-sac and few symptoms are present. Experienced clinicians are well aware of the paucity of symptoms in ectopic pregnancy with hemorrhage confined to the cul-de-sac. It is probable that free blood in this site produces little pain and that tubal distention, rupture, and edema play a significant role.

For many years the peritoneal cavity has been used occasionally as a route for blood transfusion. Questions have been raised from time to time about the efficacy of this method. That red cells do reach the peripheral blood from the peritoneal cavity has been demonstrated repeatedly.<sup>4-8</sup> Some of the best evidence for this had been derived from animal experimentation but recently work has been published which demonstrates beyond question that

human erythrocytes cross the peritoneal barrier and enter the blood stream.<sup>9</sup> Some have felt that the speed with which this transfer takes place is too slow to be useful and have pointed out other disadvantages.<sup>10, 11</sup>

Our results confirm the observations of others that red cells do cross the peritoneum and can be identified in the peripheral blood. The number we found there 48 hours after the injection of 500 ml. of blood was disappointingly small, however. The largest number discovered in the peripheral blood under these circumstances was 53,000 per cubic millimeter. Since the administration of 500 ml. of blood intravenously would be expected to augment the peripheral blood count by something in the neighborhood of from 400,000 to 500,000 cells per cubic millimeter, the effort was marked by between 10 and 20 per cent efficiency. Our other trials were even more disappointing in this respect.

Pritchard and Weisman<sup>9</sup> in their excellent experiment injected 50 to 100 ml. of the patient's own blood into the abdominal cavity after labeling it with radiochromium. With this smaller amount of blood and their technique they identified a somewhat greater percentage of injected cells in the peripheral blood than we did in our study. In 8 patients the number of cells found in the intravascular compartment at 48 hours ranged from approximately 15 to 50 per cent and averaged about 25 per cent of those injected. They carried their observations on for from 9 to 11 days and found that absorption of intact cells continued until an average of two-thirds of them eventually reached the peripheral blood. They noted, as we did, considerable individual variation with maximal absorption being reached in from 3 to 11 days. Our observations were arbitrarily discontinued at 2 days because a longer time for absorption seemed useless from the standpoint of transfusion. Pritchard and Weisman doubted the clinical applicability of the intraperitoneal route for transfusion because of slow absorption and with this we must agree.

Furthermore, observations made on the blood recovered from the peritoneal cavity indicate that when large amounts are injected it undergoes considerable destruction. In all instances, the plasma seemed to have been mostly absorbed leaving a concentrated suspension of erythrocytes and considerable free hemoglobin denoting destruction of cells. Elevations of plasma free hemoglobin in the peripheral blood at 24 and 48 hours showed that hemolysis occurred early. This was demonstrated in all patients who received 500 ml. of blood. One example which suggests the rapidity with which this may occur is that of the patient who received 570 ml. of blood and A.C.D. mixture containing a total of 72 Gm. of hemoglobin. Two days later at operation only a trace of blood remained in the abdomen. Yet the inagglutinable count before injection was 2,600 and 48 hours later it was only 2,800. This patient had a free plasma hemoglobin level at 24 hours of 38.9 mg. per 100 ml. Another patient had absorbed 64 per cent of the injected blood after 3 days. At 48 hours she had an increment in the inagglutinable count of 12,000. At the same time she had a plasma free hemoglobin value of 28.1 mg. per 100 ml. and an elevated serum bilirubin.

The fate of free blood in the peritoneal cavity seems to be that, although erythrocytes gain access to the peripheral blood, absorption of intact cells is extremely slow. A sizable portion of the blood undergoes hemolysis, sometimes rather rapidly, and the free hemoglobin is absorbed and degraded by the normal body mechanisms.

#### Conclusions

1. Citrated blood injected into the peritoneal cavity through puncture of the cul-de-sac produces transient lower and upper abdominal cramps. There is often shortness of breath, belching, and rectal pain. When the abdomen is opened one to 8 days later most of the blood has been absorbed. The bowel and omentum are coated with a thin film, however. Although no gross changes can be seen, biopsy of the pelvic peritoneum shows chronic inflammation.

- 2. When saline solution is injected by the same route, few, if any, symptoms are encountered, and there are no physical changes,
- 3. When unmodified blood is injected, the symptoms and results of examination are minimal and persist for only a few minutes. The blood clots rapidly and a considerable volume is found at operation but there is no coating of the There is slight tissue reaction.
- 4. Injection is marked by no significant change in the blood pressure, heart rate, or body temperature. There is a transitory leukocytosis and the erythrocyte sedimentation rate is elevated for as long as 4 days.
- 5. Blood injected into the peritoneal cavity in large amounts undergoes concentration. Slowly some intact cells gain access to the peripheral circulation but there is marked hemolysis and absorption of free hemoglobin.
  - 6. The intraperitoneal route is not useful for transfusion.

### References

- DeGowin, E. L., Sheets, R. F., and Hamilton, H. E.: J. Clin. Invest. 29: 693, 1950.
   Cole, W. C. C., and Montgomery, J. C.: Am. J. Dis. Child. 37: 497, 1929.
   Mengert, W. F., Cobb, S. W., and Brown, W. W.: J. A. M. A. 147: 34, 1951.
   Boycott, A. E.: Brit. M. J. 1: 567, 1910.

0

e

d

-

e

0 0

0

1

V

0

f

ľ

9 9

- Soycotte, A. E.: Bitt. M. J. 1. 301, 1310.
   Siperstein, D. M.: Am. J. Dis. Child. 25: 202, 1923.
   Hahn, P. F., Miller, L. L., Robscheit-Robbins, F. S., Bale, W. F., and Whipple, G. H.: J. Exper. Med. 80: 77, 1944.

- J. Exper. Med. 80: 77, 1944.
  7. Sipperstein, D. M., and Sansby, J. M.: Am. J. Dis. Child. 25: 107, 1923.
  8. Hollingsworth, J. W.: Proc. Soc. Exper. Biol. & Med. 87: 493, 1954.
  9. Pritchard, J. A., and Weisman, R., Jr.: J. Lab. & Clin. Med. 49: 756, 1957.
  10. Goldsmith, H. E.: Northwest Med. 31: 174, 1932.
  11. Ravenel, S. F.: J. A. M. A. 100: 473, 1933.

## TUMORS OF THE PERIPHERAL NERVOUS SYSTEM OF GYNECOLOGIC INTEREST: REPORT OF A CASE OF A NEURILEMMOMA WITHIN THE RIGHT BROAD LIGAMENT MIMICKING AN OVARIAN CYST

JOHN G. GRUHN, M.D., JOHN C. HUGHES, M.D., AND CAESAR O. ALDISERT, M.D., PITTSBURGH, PA.

(From the Departments of Pathology, Obstetrics and Gynecology, St. Joseph's Hospital)

TUMORS of the peripheral nervous system so rarely involve the reproductive organs, the pelvis, presacral area, or retroperitoneum that most active gynecologic surgeons never encounter a case. Hence it is of interest to report a case which has recently been encountered and to collect available scattered information on the subject into a convenient summary.

A 34-year-old white woman was admitted 3 weeks after noting an abdominal mass and a dragging sensation in the pelvis. System review and past history were noncontributory. The menses were normal. No urinary, gastrointestinal, or genital symptoms were noted. Physical examination disclosed a soft but firm, nontender, mobile mass, approximately 15 cm. in diameter, slightly to the right of the midline, which on pelvic examination could not be distinguished from a right ovarian cyst.

At laparotomy on April 12, 1958, two masses were found. The larger, measuring 16 by 13 by 10 cm., was located within the leaves of the right broad ligament and extended into the peritoneal reflection between the superior surface of the bladder and the anterior surface of the uterus. It was adherent to the uterus by a pedicle-like structure 1.5 cm. in diameter. A smaller, polypoid mass 3 by 2 by 1 cm. was found beneath the larger mass. It too was adherent to the uterus by a pedicle-like structure. No attachment to nerve trunks was apparent. Both masses were distinct from the ovaries. The normal left ovary and tube were left in situ. The right ovary measuring 6 by 4 by 1.7 cm. and containing a corpus luteum and several small follicular cysts was removed along with the right Fallopian tube and the appendix.

On pathologic examination the larger, partly cystic mass was completely encapsulated with a smooth surface except at two sites, one of which, measuring 1.5 cm., was raw over an area said to be adherent to the uterus, and the other of which was a smooth but irregular, tongue-shaped bosselation 4 cm. in greatest dimension, located 6 cm. from the raw area. On section through the mid-portion of the multicystic structure 600 c.c. of lemon-tinted, viscid, jellylike material was apparent. The surfaces of the cyst were smooth, glistening, and opalescent. Almost half the total mass consisted of smooth, rubbery-firm, pink-white glistening tissue, portions of which had undergone cystic degeneration. The smaller mass was completely encapsulated except at its lowermost pedicle-like region. The external and sectioned surfaces were parboiled-red in appearance. Central cystic degeneration was also apparent.

Histologic examination demonstrated an intact capsule. Neurites (nerve fibers) were found at the surface of the capsule but not within the tumor itself. The tumor consisted of varying admixtures of two types of tissue (Figs. 1 and 2). The first (Antoni type A) consisted of orderly patterns of spindle-shaped cells often in parallel rows. These cells had slightly blunted ends and elongated nuclei. The nuclei were generally placed toward the end

.

0

n

3.

9

d

S

9

d

n

r,

n

1,

1-

og

n-

d

t.

re

be

d

id

of the cells and tended to occur in parallel rows or bands, followed by a zone free of nuclei, again followed by a band of nuclei. These palisade-like nuclear formations were very prominent in some areas but barely apparent in others. Reticulum stains demonstrated thin, long, wirelike fibers passing between but not wrapped around cells. The second type of tissue (Antoni B) tended to be loose and myxoid with a haphazard arrangement of cells, no palisade formations, and included multiple areas of serous microcystic degeneration. Coalesence of cysts was common. No definite lining was apparent in cysts which were negative for mucin or hyaluronic acid. In some areas blood vessels with thick collagen sheaths were also apparent.

## Comment

Tumors of the peripheral nervous system occurring in reproductive organs, the pelvis, or retroperitoneum cannot be diagnosed as such clinically. Furthermore they occur with such rarity that even gross pathologic diagnosis may be difficult.

To orient the reader to the relevant aspects of this subject, three tabulated summaries have been included: Table I is a classification of tumors of the peripheral nervous system. Table II summarizes the reported tumors which involved genital or adjacent organs or pelvic, presacral, and retroperitoneal tissue. Table III includes the case reports of particular interest to gynecologists and obstetricians.

It is necessary only to highlight this general subject and not to recapitulate details which can be procured from original sources. Nevertheless, a summary of relevant information regarding neurilemmoma and neurofibroma is in order. The major distinctions between neurilemmoma and neurofibroma are outlined in Table I. Prior to Stout's study many authors did not make such a clear distinction; for this reason some of the earlier literature is confusing.

Verocay is credited with the first adequate histologic description of a neurilemmoma in 1908. Stout coined the name, which means "nerve sheath tumor' in 1935. By 1935 Stout had collected 194 cases from the literature and added 52 cases of his own. In 1956 Gore, Rankow, and Hanford reported 2 neurilemmomas in the retroperitoneum in a series of 389 cases, of which 138 cases (35.4 per cent) occurred outside the central nervous system. One hundred nineteen cases of neurilemmoma (86.1 per cent) occurring outside the central nervous system developed in the head, neck, or extremities. In Table II we have included 13 cases found in the pelvis or retroperitoneum. tumors are usually solitary; 3.6 per cent of the series of Gore and associates were multiple. Association with von Recklinghausen's disease has been reported in 18 per cent of cases by Stout and in 1.5 per cent by Gore. Clinically, they are rarely symptomatic save for a mass at their commonest sites of occurrence. There is usually no pain, tenderness, or paresthesia. Most of the cases occurring in the retroperitoneum or pelvis, however, commonly caused pain along involved nerve trunks. There is no relationship to trauma. They occur with equal frequency in the sexes over the whole range of age but are usually detected after the third decade.

Grossly the tumors are usually attached to nerves, but small nerves may not be noted by the surgeon. They are usually small except at sites like the retroperitoneum wherein expansion is comparatively easy. Encapsulation is the rule. Because they are soft and fluctuant, they may be mistaken for cysts or lipomas. Cystic degeneration is common; the larger the tumor, the more likely is cystic change. The cyst fluid ranges from straw colored to bloody brown in color. Our case superficially mimicked an ovarian cyst on gross inspection. The description of our case adequately summarizes the histologic appearance of these tumors. Prognostically, the neurilemmoma is always benign. It rarely recurs even when some of the capsule is left behind inadvertently or by necessity. It is dubious if malignancy ever develops from a

TABLE I. CLASSIFICATION OF TUMORS OF PERIPHERAL NERVOUS SYSTEM

NATURE	DERIVATION	TUMOR	SINGLE OR MULTIPLE	ASSOCIATION WITH VON RECKLINGHAUSEN'S	COMMENT
I. Neuroec	I. Neuroectoderm (Nerve Sheath Origin)	Sheath Origin) Related to Peripheral Nerves	erves.—		
Benign:	Schwannian cells and neurites	Neurofibroma	Often multiple	Common	Not encapsulated. Neurites intermingled. May become malignant
	Schwann cell	Neurilemmoma (schwannoma)	Characteristically solitary	1.5 to 18 %	Encapsulated. Neurites in capsule only. Invariably benign
Malignant	Malignant: Schwann cells	Malignant schwannoms or neurofibrosarcoma	Usually single	About ½ of cases associated with von Recklinghausen's disease. Reverse not true	Do not develop from neuri- lemmoma; malignant coun- terpart of neurofibroma. Mi- croscopic diagnostic criteria are subtle
II. Sympath	II. Sympathetic Nervous System (Ganglion-Cell Neoplasms) Associated With Sympathetic Ganglia.	n-Cell Neoplasms) Associ	ated With Sympath	etic Ganglia.—	
Benign:	Sympathetic ganglion cells and sheathed nerve fibers	Differentiated ganglioneuroma	Usually single	Rare	Usually in young adults. Most common in postmediastinum. Does not metastasize but may be difficult to excise in toto
Malignant:	Malignant: From undifferentiated sym- pathicoblasts to differ- entiated to ganglion cells	Ganglioneuroblastoma	Usually single	Very rare	Course and prognosis related to degree of differentiation
	Embryonal sympathicoblasts	Neuroblastoma or sympathicoblastoma	Single but usually metastasize	None	Usually in infants or children. Usually originate in adrenal. Predominantly arise in abdomen. Wide metastases. Poor prognosis.

neurilemmoma. The malignant schwannoma (neurofibrosarcoma), generally conceded to arise from Schwann cells, is usually considered the malignant counterpart of the neurofibroma.

Neurofibromas rarely occur in the pelvic region. The first examples were reported in males in 1849 by Smith. Cripps and Williamson in 1899 described

Fig. 1.

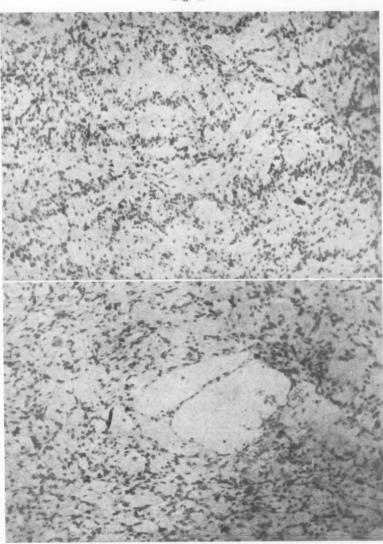


Fig. 2

Fig. 1.—Microscopic appearance of so-called Antoni type A tissue of neurilemmoma with palisading of nuclei.

Fig. 2.—Microscopic appearance of Antoni type B tissue with microcystic degeneration.

the first case in a woman of 21 in whom a fist-sized pelvic neurofibroma produced pain radiating down the leg. The recorded instances of dystocia and other specific gynecologic or obstetric problems due to neurofibromas are reviewed in Tables II and III. Pelvic neurofibromas may be clinically mistaken

TABLE II. TUMORS OF THE PERIPHERAL NERVOUS SYSTEM INVOLVING REPRODUCTIVE ORGANS OR GENITALS, ADJACENT ORGANS, OR PRESACRAL, PELVIC OR RETROPERITONEAL AREAS

		NO. OF			
ORGAN	TUMOR	CASES	AUTHOR	YEAR	COMMENT
A. Genital C	Organ Involvement				
Ovary	Neurofibrosarcoma	1	Dover	1950	
	Ganglioneuroma	1	Schmeisser and Anderson	1938	
	Ganglioneuroma	3	Cited by Stout	1947	
	(tiny nodules)		•	i	
Uterus	Ganglioneuroma	3	Cited by Stout	1947	
	(tiny nodules)		cred by stout	2021	
Vagina	Neurofibroma	1	Dover	1950	
· ug	Neurofibroma	1	Norris and Cooper	1950	
Vulva	Neurofibroma	1	Bondi	1907	
	Neurofibroma	1	Maczewski	1925	
	Neurofibroma	1	Romero	1938	
	Neurofibroma	1	Tauber	1946	
	Neurofibroma	2	Lovelady, McDonald, and	1950	
	O 11		Waugh	4000	
	Ganglioneuroma	1	Lovelady, McDonald, and Waugh	1950	
Round liga-	Neurilemmoma				
ment	(schwannoma)	1	Blondin	1927	
B. Urinary	Tract Involvement				
Bladder	Neurofibroma	1	Thompson and McDonald	1940	
Ureter	Neurofibroma	1	Ravich	1935	
0 1 1					
C. Involvem			n, or Presacral Area.—		
	Neurofibroma	2	Smith	1849	Males with neuro-
		1	Cripps and Williamson	1899	fibromatosis Fist-sized in 21- year-old woman
		1	Chiari	1898	year-old woman
		î	Versé	1915	Dystocia
		1	Pok	1916	Dystocia
		1	Sippel	1923	Dystocia
		2	Adson, Moersch, Kernohan	1939	2 9 200010
		1	DeVoe et al.	1948	
		5	Jackman, Clark, and Smith	1951	Retrorectal, 2 in women
	Neurilemmoma	1	Moreau and van Bogaert	1923	
		1	Erb	1924	
		1	Krumbein (Krekeler)	1925	
				(28)	
		1	Pescatori	1929	
		1	Pana	1931	
		1	Eichhoff and Korbseh	1932	
		1	Frank	1934	Admitted with diagnosis of ectopic preg- nancy
		1	Jackman, Clark, and Smith	1951	In male, retrorectal
		2	Ackerman (Gore)	1954	and and a contraction
		2	Gore, Rankow, and Hanford	1956	
		1	Gruhn, Hughes, Aldisert	1958	Within broad liga- ment mimicking ovarian cyst
	Malignant schwannoma	1	Ackerman	1954	
	Ganglioneuro- blastoma	1	Fels	1933	
	Ganglioneuroma	1	Stoeckel	1923	Within broad liga-
		32	Stout	1947	ment
		1	Pack and Ariel	1958	

an

n

ectal

gang

ga-

TABLE III. REPORTS OF PERIPHERAL NERVOUS SYSTEM TUMORS OF PARTICULAR INTEREST TO GYNECOLOGISTS AND OBSTETRICIANS

DATE	AUTHOR	COMMENT
1898	Beneke	First case with dystocia. Mass size of child's head in 28-year-old woman. Cesarean section
1899	Cripps and Williamson	First report of neurofibroma in female pelvis. Solid fist-sized mass in 21-year-old girl with leg pain Recovery after laparotomy
1907	Bondi	Cherry-stone-sized neurofibroma of labium
1914	Breitung	Dystocia due to two tumors in 29-year-old woman
1915	Versé	Diffuse pelvic tumor strands with von Reckling hausen's disease. Neglected dystocia
1916	Pok	Dystocia due to neurofibroma size of hen's egg Died
1923	Sippel	Dystocia. Fist-sized neurofibroma in 23-year-old woman
1923	Stoeckel	Fist-sized ganglioneuroma in broad ligament of 19-year-old girl
1927	Blondin	Schwannoma of round ligament
1927	Neumann	Hysterectomy necessary to remove tumor from 14 year-old girl
1933	Fels	Solid "unripe ganglioneuroma" in pelvis of 32 year-old woman with left sciatic pain. Recovery
1934	Frank	30-year-old woman admitted with diagnosis of ectopic pregnancy. Large retroperitoneal neurilemmoma attached to sacral plexus caused lepain
1938	Schmeisser and Anderson	200 Gm. ovarian ganglioneuroma in 4-year-ole Negro girl with abdominal swelling
1942	Duverges	Dystocia
1946	Tauber	Neurofibroma of right labium "could be confuse with Bartholin cyst"
1948	DeVoe et al.	Pregnancy complicated by 9 by 7 by 6 cm. presacral neurofibroma in 24-year-old woman
1948	Dockerty	Ependymoblastoma invaded sacrum anteriorly an joined a family of fibroids (glial, not periphera nervous system tumor)
1950	Norris and Cooper	12 by 10 cm, neurofibroma of vagina in 33-year-ol Negro woman pregnant 6 months
1950	Dover	38-year-old white woman with von Recklinghausen disease admitted for spontaneous abortion. Als had orange-sized ovarian neurofibrosarcoma an olive-sized left vaginal wall neurofibroma
1958	Pack and Ariel	Retroperitoneal ganglioneuroma, symptomatic years in 27-year-old woman
1958	Present Authors	16 by 13 by 10 cm. neurilemmoma in right broadligament clinically mimicking ovarian cyst

for uterine fibromyomas, ovarian cysts or masses, parovarian cysts, enlarged pelvic lymph nodes, psoas abscesses, anterior sacral meningoceles, and other rarer phenomena.

The relative rarity of tumors of the peripheral nervous system within the pelvis, the improbability of reaching a diagnosis on clinical grounds alone, and the difficulty in establishing a correct gross diagnosis have already been discussed. Hence one important practical point now warrants emphasis: frozen section diagnosis in the hands of an experienced pathologist should provide comforting certainty for the surgeon vexed by a perplexing case of this type at laparotomy.

## Summary

1. A case of a neurilemmoma arising in the right broad ligament and mimicking a right ovarian cyst is presented.

2. Scattered data regarding genital, pelvic, or retroperitoneal tumors of the peripheral nervous system of particular interest to gynecologists and obstetricians are compiled for ready reference.

Addendum .- Since this article was submitted, a terse review of neurofibromatosis with involvement of the genitourinary tract has appeared.44

#### References

- Akerman, L. V.: Tumors of the Retroperitoneum, Mesentery and Peritoneum, Washington, D. C., 1954, Armed Forces Institute of Pathology.
   Adson, A. W., Moersch, F. P., and Kernohan, J. W.: Arch. Neurol. & Psychiat. 41: 535, 1939.
- 3. Antoni, N. R. E.: tber Bückenmarkstumoren und Neurofibrome Studien zur pathologischen Anatomie und Embryogenese mit einen klinischen Anhang, München, 1920, J. F. Bergmann.
- 4. Beneke: Verhandl. d. deutschl. path. Gesellsch., Erst. Tagung 91, 1898.
- Blondin, S.: Ann. anat. path. 4: 328, 1927.
   Bondi, J.: Zentralbl. Gynäk 31: 1514, 1907.
- Breitung, G.: Ein doppeltes Ganglioneurome sympathicum an der Vorderfläche des Os coccygis als Geburtshindernis, Berlin, 1914, Deyhle.

- 8. Chiari, H.: Verhandl. d. deutsche path. Gesellsch., Erst. Tagung 96, 1898.
  9. Cripps, H., and Williamson, H.: Brit. M. J. 2: 10, 1899.
  10. DeVoe, R. W., Lovelady, S. B., Dockerty, M. B., and Gray, H. K.: Proc. Staff Meet. Mayo Clin. 23: 239, 1948.

- Mayo Clin. 23: 239, 1948.

  11. Dover, H.: Canad. M. A. J. 63: 488, 1950.

  12. Duverges, C. J.: Bol. Soc. obst. y. ginec. Buenos Aires 21: 576, 1942.

  13. Eichhoff, E., and Korbsch, H.: Arch. klin. Chir. 170: 246, 1932.

  14. Erb, K. H.: Deutsche Ztschr. Chir. 183: 414, 1924.

  15. Evans, R. W.: Histological Appearances of Tumors, Edinburgh and London, 1956, E. & S. Livingstone, Ltd.

  16. Fels, E.: Zentralbl. Gynäk. 57: 89, 1933.

  17. Frank R. T.: AM. J. Open & Gynäg. 27: 503, 1934.

- Fels, E.: Zentraid, Gynak, 57; 52, 1255.
   Frank, R. T.: AM. J. OBST. & GYNEC. 27: 593, 1934.
   Gore, D., Rankow, R., and Hanford, J. M.: Surg. Gynec. & Obst. 103: 193, 1956.
   Gore, I.: Cancer 5: 279, 1952.

- Jackman, R. J., Clark, P. L., III and Smith, N. D.: J. A. M. A. 145: 956, 1951.
   Krumbein, C.: Virchows Arch. path. Anat. 255: 309, 1925.
   Lovelady, S. B., McDonald, J. R., and Waugh, J. M.: Am. J. OBST. & GYNEC. 42: 309,
- 23. Maczewski, S.: Zentralbl. Gynäk. 49: 1629, 1925.
- Moreau, J., and van Bogaert, L.: Arch. franco-belges de chir. 26: 864, 1923.
   Neumann, H. O.: Zentralbl. Gynäk. 51: 2174, 1927.
   Norris, J. W., and Cooper, J. R.: J. Kansas M. Soc. 51: 128, 1950.

- 27. Pack, G., and Ariel, I.: Tumors of the Soft Somatic Tissues, New York, 1958, Hoeber-Harper.
- 28. Pana, C.: Osp. maggiore (Milano) **19**: 741, 1931. 29. Pescatori, F.: Tumori **15**: 59, 1929 30. Pok, J.: Gynäk. Rundschau **10**: 105, 1916.

- Ravich, A. Arch. Surg. 30: 442, 1935.
   Romero, J.: Rev. ginec. e d'obst. 1: 574, 1938.

- Schmeisser, H. C., and Anderson, W. A. D.: J. A. M. A. 111: 2005, 1938.
   Sippel, P.: Zentralbl. Gynäk. 47: 840, 1923.
   Smith, R. W.: Treatise on the Pathology, Diagnosis and Treatment of Neuromata, Dublin, 1849, Hodges and Smith.
- Stoeckel, W.: Zentralbl. Gynäk. 47: 33, 1923.
   Stout, A. P.: Am. J. Cancer 24: 751. 1935.
- 38. Stout, A. P.: Tumors of the Peripheral Nervous System, Washington, D. C., 1949, Armed Forces Institute of Pathology.
- 39. Stout, A. P.: Surg. Gynec. & Obst. 84: 101, 1947.

- 40. Tauber, R.: Urol. & Cutan. Rev. 50: 203, 1946.
  41. Thompson, G. J., and McDonald, J. R.: J. Urol. 43: 831, 1940.
  42. Verocay, J.: Multiple Geschwulste als Systemerkrankung am nervösen Apparate, Festschrift f. H. Chiari, Wien and Leipzig, 1908, W. Braunmüller, pp. 340-417. 43. Versé: München. med. Wchnschr. 62: 519, 1915.
- 44. Witus, W. S., Joseph, H. F., and Valk, W. L.: J. Urol. 80: 110, 1958.

### THE LEGACY OF THE PAST\*

ARTHUR T. ANTONY, M.D., BROOKLYN, N. Y.

ATTHIS, the five hundredth meeting of the Brooklyn Gynecological Society, I thought it would be appropriate to review a little of the history of our Society, emphasizing the story of the other Centennial meetings, none of which were marked by any special occasion, but all of which were attended and participated in by men whose names were familiar to all of us.

The first meeting of the Brooklyn Gynecological Society was held on April 17, 1890, with thirteen founding members present. Four other members were accepted at the second meeting, also as founding members. At this meeting the constitution and by-laws were adopted, which limited the membership to twenty-five Fellows residing in Brooklyn and New York City. needed a seven-eighths vote of all the members for election. It is, therefore, not surprising that the one hundredth meeting of the Society held on Jan. 3, 1902 (twelve years later), was dominated by founding members. The president at the time was William Maddren. The Scientific Session was opened with two case reports, the first "Exstrophy of the Bladder," and the second "Mammary Abscess Following Endermoclysis," both presented by Dr. Robert L. Dickinson. The cases were discussed by Drs. Walter B. Chase, Charles Jewett, and William Maddren. The paper of the evening was titled "Epignathus" and was presented by Dr. Charles Jewett and discussed by Drs. L. G. Baldwin and N. J. Corcoran. The only members mentioned who were not founding members were the Secretary, Dr. Frederick J. Shoop, and Dr. Clarence R. Hyde. At the executive session, Dr. Hyde moved that the Society provide a collation for members and guests at the close of the next meeting. The motion was carried and referred to the Executive Committee with power to act. Thus you can see that combining food and drink with the pursuit of scientific knowledge had an early start in your Society.

Our dinner here tonight will remind the older members present of others held at the Montauk Club by your Society in the middle and late 1930's. But even those were far from the first time our Society met here. Dr. Daily recorded in detail the entertainment of the American Gynecological Society by this Society in 1892, at which Dr. Skene was host at a sumptuous luncheon with the day climaxed by a dinner that evening at the Montauk Club. A few months later, the Society received a complete set of the Transactions of the American Gynecological Society, contained in 17 volumes, a gift from that group in recognition of the courtesies extended to its members during their visit here. This 17 volume set is still on the shelves of the Kings County Medical Library.

On Dec. 1, 1893, Dr. Frederick A. Cook, a physician with the Peary Expedition into the Arctic, addressed the regular meeting by invitation with "A Talk Upon Gynecological Matters Among the Esquimaus." I spent some

<sup>\*</sup>Presented at a meeting of the Brooklyn Gynecological Society, March 19, 1958.

time searching for this article as I thought it might be of more than historical interest, but could not find it in any of the journals publishing gynecological

In 1900, efforts by Dr. Charles Jewett to persuade the Society to surrender its autonomy to become a Section in the Medical Society, County of Kings, were to no avail. In 1897, and again in 1906, motions to open the scientific sessions of the Society to all members of the Medical Society, County of Kings, were defeated.

In 1899, the Fellowship had been increased to 30 but, in 1902, a motion to increase the membership to 45 was unanimously defeated, the gentleman offering

the motion seemingly having a change of heart.

I have mentioned the limitation of membership to emphasize the impression of exclusiveness apparent in the actions of the Society. The doors were opened only inch by inch. Not only was it difficult to become a member (some of the later most illustrious obstetricians and gynecologists of Brooklyn were not accepted as members until years after they were first proposed), but members of the medical profession at large were not welcomed at the meetings.

Dr. Walter B. Chase, a founding member, who was asked to write a history of the Society in 1914, explained this attitude by saying, "Membership was purposely limited to 25 Fellows that it (The Society) might in its own way consistently and scientifically pursue a course best fitted to the purpose for

which it was created.

"The Society grew and prospered in its chosen field, and its scientific work was given to the medical public. Though sometimes criticised for what was claimed to be an exclusive organization, it held to the belief that at that period at least, the work could most satisfactorily be carried forward under such limitations."

It was in 1902, 56 years ago, that Dr. Victor L. Zimmerman, the oldest living Life Fellow, was elected to membership. Dr. Zimmerman is living in Chatham Center, New York, and although I have not seen him for some years, we have been corresponding recently and he is still very much interested in his former colleagues and old friends.

It was in this same year, 1902, that Dr. William E. Butler demonstrated a rubber dam for use in the abdominal cavity as a protection to the intestines, also a self-retaining retractor to be used with the dam.

And, last, it was in 1902 that our Society first contributed \$100 to the

Kings County Medical Society for the use of rooms for its meetings.

The papers read at some of the early meetings discussed problems which are still controversial. In 1904 Dr. Onslow A. Gordon presented a paper titled, "Shall the Appendix Be Removed When the Abdomen Is Opened for Other Reasons?" Some of the papers were on subjects which have long since disappeared, viz., the 1906 presentation of Dr. Ralph Pomeroy, "Mechanical Means of Dilating the Cervix in Later Months of Pregnancy."

In those early years, a candidate was proposed for membership by three Fellows. Most of the proposals are on file in our records, some as notes and many on prescription blanks. There is a proposal in 1907 on one of Dr. Dickinson's professional cards. The eard states that office hours are 8:30 A.M. and 2 to 5 P.M. preferably by appointment, except Sunday and Thursday. The telephones were 4200 and 4201 Main—evidence of a very busy gynecological practice.

It was also in 1907 that Dr. Pomeroy read a case report, "Caesarean Section—Uterus Ventrofixed." The following year another case report was

read, "Caesarean Section, Uterine Inertia Caused by Ventrally Fixed Uterus," by Dr. John O. Polak.

A stated meeting of the Society was held at The Brooklyn Hospital in 1910. Dr. Dickinson described several cases of malignant disease of the cervix and uterus, after which the Maternity Department was visited, including the delivery room, medicine closet, postpartum ward, and nursery. The operating room was visited and the freezing microtome was demonstrated.

At the October, 1911, meeting, the Society resolved to approach Dr. Wendell C. Phillips, President of the Medical Society of the State of New York, proposing the establishment of a Section in Obstetrics and Gynecology in the State Society. This Section was established the following year as a direct result of the Brooklyn Gynecological Society's proposal. It was in 1911 also that amendments to the constitution increased the membership to 40, and a membership committee was formed to investigate future applicants. Each Fellow was also to have the privilege of inviting one friend to any meeting, but the same guest was not to be invited oftener than twice a year. This last was repealed some time later.

In 1913 the Secretary read a communication from the Philadelphia Obstetrical Society referring to the matter of certain advertisements appearing in the American Journal of Obstetrics and Diseases of Women and Children and asked the Brooklyn Gynecological Society to take action condemning the admission of such advertisements in the columns of the Journal. Dr. Humpstone said that the Editor of the Journal had told him that the American Journal of Obstetrics would have to go out of existence if those advertisements were not used, and moved that the matter be tabled. Unfortunately the bound volumes of the Journal do not include advertisements, but it does not take much imagination to surmise who the advertisers were. The practice was either discontinued, or, more than likely, the financial position of the Journal improved, as there is no further mention of the problem at any of the subsequent meetings.

In 1913 Dr. Dickinson wrote a letter proposing that the programs of the meetings be provided in rotation by various hospitals in Brooklyn. The first such meeting was held at The Brooklyn Hospital in 1914, the Long Island College Hospital was host for the second meeting, and then no more hospital meetings were held until after World War I was over.

The two hundredth meeting of the Society was held on May 1, 1914, with Dr. Frederick Holden presiding and Dr. Gordon Gibson as the Secretary. The paper of the evening was titled "Puerperal Infection," presented by Dr. Alfred C. Beck. It showed the results of 15 months' treatment by "judicious neglect"—this conservative treatment consisting of Fowler's position, initial cathartic, forced fluids, ice bag to the lower abdomen, ergot by mouth, and 0.5 c.c. polyvalent stock vaccine. It further showed that with few exceptions the expectant treatment of puerperal infection was wiser and gave better results than attempts to cleanse the uterus of infectious material. The paper was discussed by Drs. Pool, Baldwin, Hyde, Matheson, Chase, Mills, Knight, Robertson, Gibson, Holden, and closed by Dr. Beck. The Secretary noted that 15 members were present at the meeting, and we note that 10 members discussed the paper.

At the executive session of this meeting, the Secretary reported that he had received a letter from the Los Angeles, California, Gynecological Society, requesting literature relating to this Society for use in organizing their Society. The Secretary reported that he had forwarded such documents.

At the November, 1914, meeting an honorarium of \$100 per annum was voted to the Secretary of the Society, a custom which has continued to this day.

Interest in the Society was apparently at a low ebb in 1918, in all probability because of the war. The new president, Dr. Eliot Bishop, sent a letter to all the Fellows asking opinions as to the advisability of adjourning meetings for the duration, limiting meetings to three or four a year, or continuing as usual. He cautioned that a continuation would necessitate better attendance at meetings, that new and active members would have to be obtained, and that more discussion from the floor would have to be forthcoming. Although the January session was dropped for several years, the Society took on new life under Dr. Bishop's leadership and it continued to grow and prosper.

Dr. Frank H. Knight, a Fellow from the staff of St. John's Episcopal Hospital, was killed in action in France on Oct. 28, 1918. Resolutions in his memory were presented to the Society on May 2, 1919, thereby honoring the only member who gave his life in World War I in the service of his country.

The seriousness of the influenza epidemic of 1918 as a complication of pregnancy necessitated a symposium at the November meeting on "Influenza-Pneumonia in the Pregnant," which was opened by Dr. Pomeroy and discussed by Drs. Matthews, Holden, MacNaughton, Beck, Beach, Polak, and Pfeifer.

In the fall of 1925, the Society was saddened by the death of one of its great leaders, Dr. Ralph Pomeroy. The Society's President, Dr. Thurston S.

Welton, appointed a committee to recommend a permanent memorial.

The committee, consisting of Drs. William Sidney Smith, John O. Polak, Sylvester A. McNamara, and Adolph Bonner, reported that a meeting had been held and a portrait, a tablet, and a library fund had been discussed.

Their final decision was expressed in these words:

"Feeling that Dr. Pomeroy would have been one of the first to take the position that it is unseemly to memorialize one man without memorializing all of our distinguished deceased Fellows, it is the sense of this committee that a Brooklyn Gynecological Society Memorial Fund of not less than \$10,000 be raised for the creation and perpetuation of a Memorial room in the Library Building of the Medical Society of the County of Kings.

"This room and its furnishings and embellishments is to be given by our Society in memory of the deceased Fellows of the Brooklyn Gynecological

Society who have rendered distinguished services in our profession."

The committee's recommendation was unanimously accepted, and I might add that at the present time the Memorial Fund consists of cash and United

States Bonds with a maturity value in the amount of \$21,551.09.

In December, 1925, Dr. Charles Gordon proposed that a committee be appointed to survey and study the cesarean sections performed in Brooklyn. This was approved and Dr. Gordon was appointed chairman. On Feb. 3, 1928, Dr. Gordon submitted his report, which was discussed by Dr. Polak. A rising vote of thanks was given to Dr. Gordon and his committee for this excellent and valuable survey. The Council ordered 1,000 reprints of the report for distribution to members of special obstetrical and gynecological sections both home and abroad.

In 1929 the Council authorized Dr. Gordon to undertake a survey of

breech deliveries in Brooklyn.

The three hundredth meeting was held on May 3, 1929. Dr. George Phelan was President and Dr. Samuel Wolfe, Secretary. The scientific session was opened with two case reports, the first "Staphylococcemia After Caesarean Section With Recovery," by Dr. Jacob Halperin. The discussion was opened

by Dr. William Sidney Smith and continued by Drs. Thurston Welton, Francis B. Doyle, and Cameron Duncan. The second case report by Dr. Doyle was "Postoperative Massive Pulmonary Collapse." Discussion was opened by Dr. Charles Gordon and continued by Drs. William Sidney Smith and Samuel Wolfe.

The paper of the evening was titled "Cancer of the Corpus Uteri—Treatment With Radiation and Surgery" by Dr. William P. Healy by invitation. Dr. Healy's concluding words were, "The decision between radiation and operation in operable fundus carcinoma must for the present depend upon the circumstances in each individual case, taking into account such factors as histologic type, technical operability, stage of disease, general or constitutional and local complications."

It was at the Feb. 2, 1934, meeting that a committee was appointed by the president to study the report of the New York Academy of Medicine on maternal and fetal mortality, and to determine the responsibility of the Society in this matter and what action, if any, should be taken by it. As a result of the recommendations of this committee and with the cooperation of the Maternal Mortality Committee of the Kings County Medical Society, the May meeting each year was reserved for a discussion of maternal mortality to which the medical profession at large was invited. The first such meeting took place in 1935 with a panel presentation of what the general practitioner should know about various obstetrical complications.

The May meeting of the Society each year for the next twelve years was an open meeting devoted to maternal mortality statistics and to educational programs relating to major obstetrical problems.

During the 1930's the speakers at our meetings are familiar to even our youngest members and comprise a Who's Who in our specialty. They included Drs. Benjamin P. Watson, Edward H. Richardson, Charles G. Norris, Samuel A. Cosgrove, Nicholson J. Eastman, Herbert F. Traut, Alan F. Guttmacher, Walter T. Dannreuther, Frederick C. Irving, Isador Rubin, and many others of equal stature.

The last "special occasion" for our Society was the Fiftieth Anniversary Dinner, held at the Hotel Bossert on April 17, 1940, honoring Dr. Robert L. Dickinson who at the time was 80 years old. About 200 members and guests were present to pay homage to one of the Society's founding members, and probably the most active member during the time he was in private practice.

The four hundredth meeting of the Society took place on Nov. 5, 1943, with Dr. Samuel Lubin presiding and Dr. John J. Madden as Secretary. There were 80 members and guests present.

The scientific program was opened by a paper titled "Experience With Supravesical Extra-peritoneal Caesarean Section (Waters' Operation)" by Drs. Isadore Daichman and William Pomerance. The paper was discussed by Dr. Waters, who pointed out that "sulfanilamide is of great importance. . . But since many patients with peritonitis who have had sulfanilamide used intraperitoneally still die of peritonitis, we do not think that a transperitoneal operation with such semispecific therapy as is now available can compare with the extraperitoneal operation." Dr. Daichman in closing agreed with this, but added, "However, we must be open minded about the possible eventual efficiency of chemotherapy. It is not at all impossible that chemotherapy may eventually completely replace the need for the extraperitoneal procedure."

The second paper, "Clinical Value of Hysterography," was presented by Dr. Morris Goldberger, Associate Gynecologist at Mount Sinai Hospital.

This brings us up to moderately recent times, with which most of us are personally acquainted. I think it appropriate for me to pause here to allow someone else, at some future time, to tell the story of the recent past, noting the Society's interest in sponsoring conferences on pelvic malignancy and perinatal mortality.

As I mentioned previously, a history of our Society was written by a founding member, Dr. Walter B. Chase, in 1914, 44 years ago. His closing remarks are as pertinent today as they were then:

"I venture the statement that exchanges of opinion and experience within our own circle have made us individually better gynecologists and wiser obstetricians, whereby doubts and errors have been dispelled, judgment matured and invigorated, and the narrow path of real success lifted to a higher plane.

"The past of the Brooklyn Gynecological Society is secure, its future rests with you and those who follow you. The history of the past, the hope and inspiration of the present, point the way to higher and better things."

Dr. Warren A. Lapp has been compiling a history of our Society. I am greatly indebted to him for allowing me to use portions of the material he had gathered.



### DEPARTMENT OF CURRENT OPINION

Clinical Problems

### POSTMENOPAUSAL UTERINE BLEEDING

### Case Presentation

Mrs. A. V., age 52, white, gravida i, para 0, had her last menstrual period at the age of 48 years. Three years later, at age 51, she had a 7 day episode of uterine bleeding. The bleeding was moderate in amount but much less than she had ever experienced at menstruation. Examination at that time revealed a normal cervix, a uterus that was of normal size, anterior, regular, and freely movable, and normal tubes and ovaries. On general examination no abnormalities were found. The blood pressure was normal. Blood studies revealed no abnormalities. A cytosmear was negative for cancer. Curettage and conization of the cervix under anesthesia were performed. The report from the Department of Pathology was chronic cervicitis, atrophic endometrium.

Six months later, at the age of 52 years, the patient again had uterine bleeding, 3 days in duration and spotting in character. A cytosmear for cancer was negative. The findings were identical to those of 6 months previously.

Problem: Would you discuss this situation and present your method of management?

### Consultation

R. W. TE LINDE, M.D., BALTIMORE, MD. PROFESSOR OF GYNECOLOGY, THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE; CHIEF GYNECOLOGIST JOHNS HOPKINS HOSPITAL

This case presents the problem of recurrent uterine bleeding in a postmenopausal woman in whom the first curettage and cervical conization failed to explain the cause. It is a problem which should not be taken lightly; nor should one rush in and perform a hysterectomy and double salpingo-oophorectomy without further investigation. In general, it is a good rule to know as exactly as possible the pathological condition for which one is operating.

Several years ago I made a clinicopathological study of the causes of postmenopausal bleeding. In slightly over 50 per cent of the postmenopausal bleeders the source of the bleeding was malignancy somewhere along the generative tract. In approximately 35 per cent of the cases, the cause was cervical cancer and, in about 15 per cent, carcinoma of the endometrium. The other malignant causes were sarcoma of the endometrium, sarcoma in myomas, and ovarian malignancy. These percentages would not hold today because so many postmenopausal women present themselves with bleeding due to the administration of hormones. Nevertheless, malignancy still remains a likely possibility in every case of postmenopausal bleeding and the diagnosis should be ruled out or established in every case. In the above history there is no mention of hormonal therapy and I will assume that no hormones were administered. Also in the history, the statement is made that the bleeding is uterine in origin. Germane to the subject, however, is bleeding from postmenopausal vaginitis. It is one of the most common causes of bleeding from the vagina in elderly women and the patient simply presents herself with vaginal bleeding and the vagina, as well as the upper genital tract, must be considered as the possible origin. bleeding is from vaginitis, it is usually a blood-stained purulent discharge, but not always, because vascularized adhesions in the senile vagina may at times be the source of bright, fairly profuse bleeding. Speculum examination will usually disclose the bleeding spots in the vagina but one should remember that the presence of bleeding from the vagina does not exclude the possibility of bleeding from higher in the generative tract.

What are the possibilities in the above case? There is the possibility that an endometrial lesion responsible for the bleeding was missed at the original curettage. It is even possible that a minute cervical lesion was missed on examination of the excised cone. Small ovarian neoplasms can exist in normal-sized ovaries and cause uterine bleeding, particularly granulosa and theca cell tumors. Finally, there is the rare possibility of carcinoma of the tube.

Let us first consider the possibility of an endometrial lesion being missed at the first curettage. Small endometrial carcinomas have been missed even when a seemingly thorough curettage was done. This is relatively easy to do when the carcinoma grows in polypoid form as it sometimes does. It is still easier to miss a benign endometrial polyp. Most of us have had the experience of performing a hysterectomy for what was thought to be recurrent functional bleeding on a woman who had previously had a curettage, only to find an endometrial polyp which could have been removed by a much simpler procedure. For the past several years, it has been our practice to search the uterine cavity with a special small polyp forceps each time a curettage is done. We have often been rewarded with a polyp which was responsible for the bleeding.

In the case at hand the interior of the uterine cavity should be carefully explored at the time of the curettage for an irregularity, with the possibility of a small submucous fibroid in mind. The fact that the uterus is normal in size and regular in outline does not exclude this possibility. Nor is this possibility excluded because the patient is postmenopausal. Although it is rare for a fibroid to migrate from the myometrium into the uterine cavity after the menopause, it can and does occur. We have seen even profuse hemorrhage caused by this in women much older than the one under consideration.

The negative cytological smear should not give one a sense of security when considering endometrial cancer. Falsely negative smears are much more common in the presence of endometrial cancer than in cervical neoplasm. The reason for this is twofold. The individual cells in endometrial cancer are often much less malignant-looking than the cells of epidermoid cancer. Also, cervical stenosis of various degree is common in postmenopausal women and few or even none of the malignant cells may find their way into the vagina.

The likelihood of an early cervical cancer being missed when the cytological smear and the cone are negative is very slight. We have had a few cases of

carcinoma in situ missed on microscopic examination of a cone but in such instances the smears have remained positive or suspicious. Nevertheless, when curettage is done I would do a ring biopsy of the cervix upon this patient.

What of the possibility of an ovarian neoplasm? About one fourth of our ovarian tumors occurring after the menopause were found to have at least a slight show of blood from the vagina. The percentage of bleeding would be even higher if based on only malignant ovarian tumors. The bleeding associated with the ordinary ovarian cancer is usually present when the neoplasm is advanced. It may be explained on the basis of bloody ascitic fluid discharging through the tubes and into the uterus or by an extension of the malignant growth into the uterine cavity. In the case under consideration, the ovaries were noted to be normal in size so that if an ovarian malignancy is present it would have to be a functioning tumor such as a small granulosa or theca cell tumor within a normal-sized ovary. We have had 2 such cases in our clinic. I am reminded of an old article in the German literature by Neumann. performed a vaginal hysterectomy on a woman with postmenopausal bleeding which was not explained on the basis of the endometrial findings. Two years later the woman presented herself with hopeless ovarian malignancy. From this experience, Neumann concluded that a hysterectomy and double salpingooophorectomy should be done on all women with postmenopausal bleeding not explained on sound endometrial or cervical pathology. Such a deduction based upon this experience in a single case is, in our judgment, unwarranted. Nevertheless, Neumann's case does teach us a lesson. When an adequate explanation of the bleeding is not at hand on the basis of the endometrial or cervical findings, the patient should not be dismissed but followed with careful palpation of the ovaries at not too long intervals.

Finally, the possibility of tubal carcinoma must be considered. This neoplasm with a high mortality is a silent grower and frequently the first and only symptom is a bloody discharge. This, then, is another reason for careful adnexal palpation in all cases of postmenopausal bleeding.

Since there are these many possibilities of a serious lesion being responsible for the uterine bleeding, the reader may quite properly ask, "Why not proceed directly with a hysterectomy and bilateral salpingo-oophorectomy?" The answer is that if one makes it a rule to perform major operations in cases such as this, he would perform many unnecessary hysterectomies. If we are quite honest with ourselves, we will be forced to admit that there are many cases of postmenopausal bleeding that are never satisfactorily explained on solid pathological grounds. The bleeding often stops as mysteriously as it starts. is not to say that I have never removed a postmenopausal uterus in which I could not find the cause of bleeding. I have done so in a few instances when the bleeding had been very persistent and/or quite profuse. In the case in question, the bleeding has been neither prolonged nor profuse. Therefore, my management of this patient would be to perform another curettage with use of the polyp forceps and including a ring biopsy of the cervix. Under the anesthesia I would again carefully palpate the adnexa. If all the findings of the above procedures were found to be negative, I would keep the patient under observation. If bleeding recurred another time, I would proceed with a hysterectomy and bilateral salpingo-oophorectomy. Whether this operation is done abdominally or vaginally would depend upon the operator's judgment of his own ability to remove the uterus and adnexa vaginally. If there is any doubt in his mind as to his ability to handle the procedure safely and completely per vaginam, he had better approach the operation through the abdomen. After removal of the specimen, the endometrium and ovaries should be carefully studied histologically, but the operator should not condemn himself if no satisfactory pathological explanation for the bleeding is found. He will have done his best to discover it, and failing, he will have played the game safely for the best interest of his patient.

RALPH A. REIS, M.D., CHICAGO, ILL.
PROFESSOR, DEPARTMENT OF OBSTETRICS
AND GYNECOLOGY, NORTHWESTERN UNIVERSITY
MEDICAL SCHOOL; PASSAVANT MEMORIAL
HOSPITAL

This 52-year-old postmenopausal patient presents a relatively common clinical problem, the successful management of which requires the carrying out of carefully planned management and procedures.

Postmenopausal bleeding means pelvic malignancy unless and until proved otherwise. Therefore, when a patient presents herself with the above problem, all diagnostic procedures aimed at either proving or eliminating a tentative diagnosis of malignancy must be carried out. This seems to have been done quite adequately in the case under discussion as evidenced by a negative physical examination, negative bimanual examination, and by the statement that the cervix, uterus, tubes, and ovaries were normal to the examiner.

One must assume that the detailed and careful vaginal examination included a Schiller test of the cervix and vagina. Such a test has value in pointing out possible areas of mucosa which do not take the iodine stain. Such areas immediately become doubly suspicious of malignancy.

One must further assume that the vaginal mucosa was carefully inspected in its entirety. Specific mention is made of this point because thorough vaginal inspection is frequently omitted. Too often the examiner is overanxious to visualize the cervix, and too often the vaginal mucosa is not carefully inspected. Such complete inspection of the vaginal mucosa cannot be carried out with the ordinary bivalve speculum unless it is rotated laterally in both directions in order to expose the anterior as well as the posterior vaginal mucosa.

The present-day emphasis on the various laboratory procedures for the diagnosis of genital malignancy should not be overstressed nor relied upon entirely. Cervical lesions can be missed by the biopsy punch, and endometrial lesions frequently defy detection by vaginal, cervical, or endometrial cytosmears. Even curettage is not infallible since it has been shown that 5 to 10 per cent of endometrial carcinomas can and are missed by the curette. Visualization of the cervix and vagina to eliminate benign causes of postmenopausal bleeding and to evaluate the mucosa in possible relation to hormone stimulation or deprivation is most essential.

The value of the cervical cytosmear is that of a screening procedure. It cannot be used as a diagnostic procedure upon which definitive therapy should be based. The reliability and usefulness of this test in cervical carcinoma is beyond question since it is approximately 95 per cent accurate. However, the problem is much different in the presence of endometrial carcinoma in which condition false-negative reports run as high as 30 to 40 per cent. This error can be greatly reduced by the use of direct endometrial smears or aspiration of the uterine cavity. Both of these latter carry a reported accuracy of over 85 per cent. The carrying out of either of these procedures involves invasion of the uterine cavity. Such invasion carries the possibility of causing an intrauterine infection which might seriously delay definitive therapy. It is for this reason that thorough curettage under anesthesia, as was carried out in this patient, is the more desirable and more direct approach.

s

rf

S

Assuming that all of these procedures were carefully done and all proved negative for malignancy before the patient had been discharged, what shall be the course of action now that the bleeding has recurred? This patient should be meticulously and thoroughly re-examined and evaluated de novo. Previous findings should not be relied upon, and each procedure must be carried out again. When this patient is scheduled for curettage, she should also be scheduled for possible hysterectomy. The repeat cytosmear together with the original conization of the cervix have eliminated cervical carcinoma. Nevertheless, the repeat curettage should again be a fractional one and any and all tissue removed from the cervix by the curette should be examined by frozen section while the patient is still in the operating room. Curettage and exploration of the uterine cavity with polyp forceps may elicit a definite benign cause for the uterine bleeding. If a benign lesion, usually an endometrial polyp, is found, no further surgical attack is indicated.

On the other hand, if the curette and/or polyp forceps fail to disclose the cause of the bleeding, hysterectomy should be performed. The rationale for the performance of hysterectomy upon a postmenopausal patient under these circumstances seems quite obvious. The postmenopausal uterus is at best a potential source of danger to the patient. Certainly a postmenopausal uterus that has twice bled without demonstrable cause is an actual source of danger to the patient. The danger and the risk of hysterectomy under these circumstances is certainly no greater than the risk of multiple repeat curettages.

Hysterectomy under these circumstances, namely, in a postmenopausal woman with repeat uterine bleeding and no demonstrable cause for the bleeding, is definite curative therapy. It removes the source of the bleeding, eliminates the possibility of undetected corpus malignancy, gives the patient security and peace of mind, and, last and more important, gives the operator an opportunity to evaluate carefully the tubes and ovaries. Bilateral salpingo-oophorectomy should be carried out in every postmenopausal woman who is undergoing hysterectomy for unexplained bleeding.

Such hysterectomy as here described may be carried out either vaginally or abdominally. The decision as to the method of approach for the hysterectomy should be made *in* the operating room provided that the operator is equally skilled in vaginal hysterectomy and abdominal hysterectomy. If his skill is truly equal, he will remove the tubes and ovaries under the same circumstances following vaginal hysterectomy as he will following abdominal hysterectomy.

There is still one point in connection with this case which should be discussed. Postmenopausal bleeding is very frequently due to hormone therapy or to withdrawal bleeding and occasionally to ingestion of estrogens with food or absorption from certain cosmetics. It is not mentioned in the protocol whether or not this patient had been receiving any hormone therapy. Even if she had received such therapy, the recurrence of bleeding warrants a complete diagnostic work-up and definitive management as outlined. It is not good practice to label such bleeding as hormonal, nor is it safe to permit such a patient to continue without definitive management.

### Editor's Comment

Both Consultants brought up the question of the possibility of the patient's receiving estrogenic therapy. She had not been given such therapy. The question is excellent because postmenopausal bleeding is quite frequently the result of such therapy.

As a follow-up report, this patient was hospitalized a second time for investigation of the cause of the bleeding. "Fractional" curettage and conization were performed. Frozen section preparations were made and reported

by the Department of Pathology as negative for malignancy. Following the curettage, the interior of the uterus was explored with a polyp forceps without any tissue being obtained. The cause of the bleeding remained unexplained. In view of the fact that this was the second episode of postmenopausal bleeding, vaginal hysterectomy and bilateral salpingo-oophorectomy were performed. The uterus and tubes and ovaries were grossly normal. Microscopic study revealed no malignancy and no cause for the bleeding was apparent.

One of the Consultants stated that hysterectomy and bilateral salpingooophrectomy is an acceptable procedure after two episodes of postmenopausal
bleeding in those patients in whom no cause for the bleeding could be determined. The other stated that under these circumstances such a procedure might
be done after a third episode of bleeding. These two views are not too far
apart. Both Consultants believe that postmenopausal bleeding is a symptom of
significance, that when it occurs all possible diagnostic procedures should be
performed, that if it recurs the diagnostic procedures must be repeated, and
that if no cause is found, definitive therapy should be instituted at some stage—
one recommends after the second and the other after the third episode of bleeding. The important thing of the two Consultants' opinions is the fact that
neither would permit a patient with this symptom to continue to have episodes
of postmenopausal bleeding without eventually removing the uterus, tubes, and
ovaries, even if no cause for the bleeding could be demonstrated. Most of us
agree with this premise.

I would like to stress the utilization of frozen-section examination of the tissue obtained by curettage and conization. With proper technique and willingness on the part of the pathologist, this can be most useful and may permit immediate and proper definitive treatment.

### CARCINOMA OF THE BREAST AND PREGNANCY

ie it d. g, ie d

al

P-

it

r

f

d

ıt

S

d

IS

0

### Case Presentation

Miss J. B. registered Jan. 18, 1954, at the age of 25, for premarital examination and advice; she was to marry 2 weeks hence. Examination by systems failed to reveal abnormal findings, and routine laboratory studies of blood and urine were within normal limits. Routine roentgen study of the chest was reported as negative.

The patient was next seen as Mrs. T. B. on July 7, 1954, with the history of her last regular menstrual period beginning April 21, 1954. Her prenatal period was uneventful and on Feb. 1, 1955, she was delivered spontaneously of a normal infant. She was discharged as completely recovered on April 25, 1955. She breast-fed her infant.

The next admission of this patient was Oct. 14, 1957, when she complained of a lump in the outer lower quandrant of her right breast, present for one week. She was 27 years of age, gravida ii, para i, her last normal menstrual period having been March 1, 1957. Examination of the breast revealed a firm, freely movable mass, the size of an average green olive. No regional adenopathy was discovered. A normal pregnancy of about 32 weeks was progressing uneventfully. The following day a frozen section of the removed lump revealed scirrhous cancer, and a radical mastectomy was performed. The pathologist's report of his examination of the breast and attached nodes and fat showed (a) lymphatics, no tumor, (b) lymphoid and fatty tissue, no tumor, and (c) carcinoma simplex. She recovered from the surgical procedure without complication and returned home on Oct. 22, 1957, the eighth postoperative day. She was delivered of a normal infant spontaneously on Feb. 8, 1958. She remained under observation, returning on March 21, 1958, for her postnatal visit, and every 6 weeks thereafter for breast examination. On Nov. 13, 1958, when the baby was 9 months old, thickening in the upper outer quandrant of the left breast was discovered. No definite mass or regional adenopathy could be demonstrated, but the patient was hospitalized at once for further study. Skeletal x-ray series were reported as follows: "There is an area of decreased density in the greater trochanter of the left femur. This has the appearance of osteoporosis; however, metastatic growth cannot be ruled out."

Frozen section performed on Nov. 18, 1958, was reported as "Intraductal carcinoma, definite invasion not demonstrated." Further study revealed microscopic areas of invasion. Radical mastectomy was performed but tumor could not be demonstrated in lymph nodes. Three days later bilateral oophorectomy was performed through the vagina in preparation for hormone therapy if further evidence indicated residual or metastatic disease.

## Problem: 1. Would you discuss the following questions pertaining to the specific patient presented here?

a. Was the radical mastectomy the procedure of choice and is it a safe procedure to perform upon a pregnant mother?

b. Should x-ray therapy to the cervical, intrathoracic, and axillary glands and tangentially to the chest wall have followed

immediately in spite of pregnancy or should it have been instituted after delivery?

- c. Was the castration justified?
- d. What therapy would you recommend if disease persists or recurs?
- 2. Would you discuss in general the problem of breast cancer in relation to coexisting pregnancy and in relation to subsequent pregnancy?

### Consultation

L. M. RANDALL, M.D., ROCHESTER, MINN. PROFESSOR OF OBSTETRICS AND GYNECOLOGY, MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH; SENIOR CONSULTANT IN OBSTETRICS AND GYNECOLOGY, THE MAYO CLINIC

Immediate radical mastectomy was the treatment of choice in this patient and the presence of pregnancy should not affect the risk to the mother. It would seem most inadvisable to allow the patient to carry the lesion for the additional weeks of pregnancy after it had been disturbed by manipulation and biopsy. Further, it has been demonstrated that radical mastectomy, during the function of lactation, carries the least favorable prognosis of any group of patients with cancer of the breast. In one group of 39 such patients, involved axillary nodes were present in 88.6 per cent and no patient survived 5 years. This is in contrast to nodal involvement of 54.1 per cent among 37 patients who experienced radical mastectomy for carcinoma during pregnancy and in whom the survival rate was much more satisfactory. Thus, when one speaks of carcinoma of the breast in association with pregnancy, those patients who are in the period of lactation should be considered separately. Carcinoma of the breast is one of the more aggressive neoplasms. Accordingly, unless the lesion is inoperable or the condition of the patient precludes radical mastectomy, the operation should be performed immediately when the diagnosis is made by microscopic examination. It is true that the infant may be subjected to the risk of premature birth at 32 weeks of gestation. As mentioned above, however, this risk is significantly less than the risk to the mother from delay in treatment to the termination of pregnancy, following either induction or spontaneous onset of labor, when mastectomy would be performed on a functioning breast.

There is reasonable doubt that radiation treatment given postoperatively will materially alter the prognosis. Opinions on this point may differ for they will be based on comparison of different groups of patients of varying composition. The experience in our institution indicates that, when axillary nodes were involved, treatment with radiation did not improve the rate of cure. Indeed, those patients in this group who received no such treatment exhibited a slightly higher survival rate. When no nodal involvement was present the same circumstances prevailed. Perhaps this is to say that extirpation of the nodes is sufficient local treatment and that, with or without involvement of the nodes—if the lesion has spread beyond—radiation treatment to the operative site and adjacent areas will be of no avail. Obviously, the above is an expression of opinion based on the experience here. If it were the practice and considered opinion of the surgeon responsible for the care of this patient that radiation should be administered, then it should be carried out regardless of the presence of pregnancy. Care in technique and screening should protect the infant.

Castration among women in the premenopausal age group, suffering from carcinoma of the breast, may be discussed first from the standpoint of prophylaxis. By this is meant the surgical removal of the ovaries shortly following or at the time of mastectomy. This procedure is quite debatable for presently there is insufficient evidence that it delays or prevents metastases or favorably affects the rate of survival. Evidence at this time would indicate that carcinoma of the breast among these women offers essentially the same prognosis as among women in the older age group in spite of the presence of functioning ovaries. Included in the experience at this Clinic are 115 patients operated upon for carcinoma of the breast who had experienced oophorectomy for benign conditions one or more years previously. Of these 115 patients, 57.4 per cent were found to have involvement of the axillary nodes, identical with the entire series, and the survival rate was the same as in the total group. Some surgeons do advocate prophylactic castration, however, and it is to be hoped that a statistically significant number of cases will ultimately be accumulated in order to allow documentation of the merit of the procedure. When recurrence or metastases are detected in premenopausal women it is believed that castration by surgical removal of the ovaries should be the first step in treatment. Thus, in my opinion, when castration was performed in this patient it was amply justified. In our experience, about 40 per cent of these patients will give evidence of lack of progression or actual regression of the lesions in the succeeding few months. this is true, further treatment is withheld pending the results of close observation. Exception may be made in the presence of osseous metastases in weightbearing areas when pathological fractures may be anticipated. Under these circumstances, radiation therapy to the obvious lesions is administered. is now confronted with the problem of palliation to prolong life, relieve pain, improve the general condition, and support the morale of the patient and the relatives, but with little or no prospect of cure of the disease. Thus the rapport between the physician and the patient and relatives becomes a problem indeed. There is need for much understanding, experience, time, and patience. speak of "treatment" in relation to medications of various sorts but the nuances of "management" of these situations are many. Programs of treatment have run the gamut of oophorectomy, adrenalectomy, hypophysectomy, radiation, administration of steroids, chemotherapy, etc. Each of these or combinations thereof have resulted in significant palliation for some time in a goodly number of patients. There is an understandable temptation to employ many modalities of treatment simultaneously or in rapid sequence and perhaps in an occasional instance such is justifiable. However, in general, one attempts to select a sequence of treatment that seems appropriate for the given patient, proceeding from one to another when the palliative effect of a therapeutic agent wanes. This seems preferable to a program that exhausts all therapeutic measures in one intensive program.

Clinical trials of various steroid and chemotherapeutic agents continue with the hope that more effective weapons will appear for palliation in these patients. The preliminary report of Blackburn and Childs in the March 4, 1959, issue of the Proceedings of the Staff Meetings of the Mayo Clinic is an example. They reported a double-blind study that compared the results of the administration of testosterone propionate with one of the analogues of testosterone, 2-alphamethyl-dihydrotestosterone, in the treatment of metastases following primary carcinoma of the breast. Using direct measurement of tumor size as a criterion, they observed regression of lesions in 3 of 21 (4.7 per cent) patients treated with testosterone propionate. Of 27 patients treated with the analogue, regression occurred in 12 (45 per cent), 3 of whom had primarily visceral metastases, 8 osseous disease, and one cutaneous lesions. Obviously, this experience is small and the report preliminary, but such results do give some hope for the

future. I have employed the term "premenopausal" which brings up the problem of when does the menopause actually occur. Quite certainly it is not accurately dated solely on the time when menstruation last occurred, for ovarian production of estrogen is known to persist well after this episode. This is of importance, first, from the standpoint of castration when metastases appear in women in this age group and, second, because, among women well past the period of ovarian function, the administration of estrogens has been of benefit for palliative treatment while in those in whom function of the ovaries continues, testosterone, or one of its analogues, is to be employed.

Naturally, the question of future pregnancies will arise among women who have undergone radical mastectomy for carcinoma of the breast. Subsequent pregnancy does offer a possible hazard. Therefore, it seems well to advise delay of 3 to 5 years following the operation in order to evaluate the situation in so far as possible. Among 82 such patients the 5 year survival rate was 63.5 per cent. This is actually a higher rate than the over-all 5 year survival of the entire group of 1,900 reported in that series of patients, namely, 59.3 per cent. However, these 82 patients must be considered as a "select" group for they had proved their survival for a significant period of time before the pregnancy occurred and were, therefore, presumably free of disease.

The brief discussion of this case report is, of necessity, an attempt to depict an evaluation of a complicated problem in a nutshell, so to speak, for this particular combination of circumstances. When one considers the entire group of women afflicted with carcinoma of the breast, numerous factors will influence the selection of treatment and the prognosis, such as the grade of malignancy (not stated in this case), the general condition of the patient, and the size and location of the lesion in the breast together with the unknowns of aggressiveness of the tumor versus host resistance:

HERBERT E. SCHMITZ, M.D., CHICAGO, ILL. PROFESSOR AND CHAIRMAN OF THE DEPARTMENT OF OBSTETRICS AND GYNECOLOGY, STRITCH SCHOOL OF MEDICINE OF LOYOLA UNIVERSITY; CHAIRMAN OF THE DEPARTMENT OF OBSTETRICS AND GYNECOLOGY MERCY HOSPITAL, LOYOLA UNIVERSITY CLINICS; DIRECTOR OF THE MERCY HOSPITAL INSTITUTE OF RADIATION THERAPY; CHIEF OF STAFF, LEWIS MEMORIAL MATERNITY HOSPITAL

I shall endeavor to comment on this case in the order in which it is related. Immediate biopsy of all breast lesions is indicated, as patients and physicians tend to delay investigation of breast masses or other symptoms believing them to be part of the normal sequence of events of pregnancy. Abortion does not benefit the subsequent course of breast cancer and its incidence is not increased because of mastectomy.

X-ray therapy need not be utilized in this instance because it is questionable that it is of any benefit following radical mastectomy without proof of lymph node invasion, although in some instances the cells permeate the blood vessels and metastasize per the blood stream. It is impossible to give an adequate radiation dose to the stripped chest wall and the chance of irradiation of local recurrences is then lost. The irradiation to the fetus with the pregnancy at 32

weeks would be dangerous and undesirable for the fetus. The same arguments are valid for not irradiating the chest wall after delivery of the fetus, as there are no increased survivals of significance that indicate an advantage for the irradiated group.

If both breasts had been removed as a routine, as advocated by George Pack, this patient might have been spared her second experience, although only 5 per cent of cases have disease in the opposite breast subsequent to unilateral radical mastectomy. It would add little to the original risk and none to the convalescence, so it should be considered.

Castration adds nothing to survival figures when used prophylactically, but is of benefit in recurrence when an estrogen withdrawal program is being carried on. It is a preliminary to androgen therapy and adrenalectomy, or hypophysectomy, if the patient's disease is considered as amenable to this therapy. According to evidence collected by White and others, the end results obtainable by this regimen are equal to those obtained in the nonpregnant patient.

Regarding future pregnancy, I agree with the results of a national survey which demonstrated that, if the disease was eradicated by the first procedure, future pregnancy had no ill effect, while, if disease remained, it would manifest itself in spite of no future pregnancy.

### Editor's Comment

There is considerable difference of opinion regarding the management of patients with carcinoma of the breast and efforts are being made by numerous groups to determine the best procedures. The fact that a patient is pregnant at the time the cancer is diagnosed and the fact that some of the patients with breast cancer desire to have pregnancies in the future pose additional problems that must receive consideration. Here, also, there are differences of opinion. Until real proof has been established, one must carefully study the statistical data available and consult with those who have had vast clinical experience before selecting management procedures—even then there may be not be agreement.

In the case presented here both Consultants state that radiation therapy to the chest wall in all probability will not increase the cure rate and this is in keeping with the majority of statistical evidence. Despite this, there are occasions when the surgeon in charge of the management may urgently desire that radiation therapy be employed. Before such therapy is started, its possible effect upon the fetus must be considered. One Consultant notes that such therapy administered to a patient 32 weeks pregnant would be hazardous to the fetus. The other Consultant believes these hazards can be obviated by eare in technique and proper screening, although I gather that he would be rather loath to employ this type of therapy in the case presented.

I am convinced that most surgeons would prefer that a patient who has had a breast cancer not become pregnant in the future. I am equally convinced that most would permit pregnancies in those patients who have been successfully treated and who have remained free of disease for 5 years. The two Consultants agree on this point.

The problem of prophylactic castration at the time of, or shortly after, treatment of the primary lesion has been extensively discussed in the past few years and there are those who advocate it and some who hold the view expressed by the two Consultants, namely, that castration be reserved until metastases have developed. Surgical castration is preferable to radiation castration if the condition of the patient permits.



# Reviews and Abstracts EDITED BY LOUIS M. HELLMAN, M.D.

### BOOKS RECEIVED FOR REVIEW

- Reproduction in Domestic Animals. By H. H. Cole and P. T. Cupps. Volume I, 651 pages. New York, 1959, Academic Press, Inc. \$14.50.
- Strahlenbehandlung in der Gynäkologie. By Julius Ries and Josef Breitner. 219 pages, 60 figures. München and Berlin, 1959, Urban & Schwarzenberg. DM 32.
- A Textbook of Medicine. By Russell L. Cecil and Robert F. Loeb. Tenth edition, 1,665 pages, 182 figures. Philadelphia, 1959, W. B. Saunders Company. \$16.50.
- Textbook of Pediatrics. By Waldo E. Nelson. Seventh edition, 1,462 pages, 428 figures. Philadelphia, 1959, W. B. Saunders Company. \$16.50.
- That the Patient May Know. By Harry Dowling and Tom Jones. 139 pages, 4 plates. Philadelphia, 1959, W. B. Saunders Company. \$7.50.
- Transplantation of Tissues. Edited by Lyndon A. Peer. Volume II, 690 pages, 252 figures. Baltimore, 1959, Williams & Wilkins Company. \$20.00.

### SELECTED ABSTRACTS

### The Lancet

Vol. 2, Oct. 11, 1958.

\*Antia, F. P., Bharadwaj, T. P., Watsa, M. C., and Master, J.: Liver in Normal Pregnancy, Pre-eclampsia, and Eclampsia, p. 776.

Antia et al.: Liver in Normal Pregnancy, Pre-Eclampsia, and Eclampsia, p. 776.

In this study from Bombay, needle biopsies of the liver were done on 41 pregnant patients. Ten of these patients were normal, 16 had pre-eclampsia and 15 had eclampsia. Needle biopsies were performed in the normal patients in the ninth and tenth months of pregnancy and in the others between the seventh and the tenth month. The parity and ages of the patients were roughly the same in the normal and abnormal groups. In normal pregnancy the material obtained by means of the Vim Silverman needle did not differ sig-

<sup>\*</sup>This article has been abstracted.

nificantly from normal liver. In pre-eclampsia the liver was also normal except for slight anisocytosis and anisonucleosis. The sinusoids contained hyperplastic reticuloendothelial cells and there was a distinct increase in the number of cells showing binucleation. In eclampsia the changes were similar to those seen in pre-eclampsia except in 5 instances. In 2 of the latter there was profound destruction in the portal region. In the immediate periportal area there was massive destruction of liver cell plates, leaving only isolated groups of cells. These focal changes were similar to those described by Sheehan (in Toxemias of Pregnancy, edited by J. Hammond, F. J. Browne, and G. E. W. Wolstenholme, page 19). In one case, the lesion was similar to the diffuse type also described by Sheehan. In another case there was much loosening of liver cell plates and isolation of single or small groups of cells from each other. The cells were of various sizes and shapes and some were binucleated. In the fifth patient there was gross destruction of liver parenchyma and this patient probably had fulminant infective hepatitis. Pronounced hepatic lesions thus were found in only 5 patients, one of whom probably had infective hepatitis. The paucity of abnormal histology may be explained by the fact that the material was obtained by needle biopsy rather early in the course of the abnormality and the hepatic alteration may not be found until the last day or two of life. Again excepting the instance of hepatitis, the type and severity of the hepatic lesion could not be correlated with any of the clinical or laboratory data. For example, hematological values did not differ significantly between the 3 groups, alkaline phosphatase values tended to be higher in the more severe grades of toxemia but cephalin flocculation and thymol turbidity were abnormal only in some, and bromsulphalein retention, serum bilirubin, and nonprotein nitrogen values did not indicate the type or degree of toxemia.

DAVID M. KYDD

Nov. 8, 1958.

5

\*Butler, Elizabeth A., and Flynn, F. V.: Proteinuria of Renal Tubular Disorders, p. 978.

### Butler and Flynn: The Proteinuria of Renal Tubular Disorders, p. 978.

Proteinuria as it appears in a variety of conditions was analyzed by means of paper electrophoresis. In 39 patients with more common causes of proteinuria (nephritis, nephrosis, diabetes mellitus, congestive heart failure, toxemia of pregnancy, lupus, renal calculi with infection, cirrhosis of liver, fever due to upper respiratory infection), albumin was the predominant protein. In a given condition considerable variation in the pattern was found but in general the proteins of lower molecular weight predominate over the  $\alpha_2$  and  $\gamma$  globulins. In 7 healthy adults, the pattern was faint because of the small amount of protein, but albumin was clearly the largest single fraction though the sum of the globulins appeared to be greater. In 40 patients with multiple myeloma usually a solitary peak was found in the  $\beta$  to  $\gamma$  region but sometimes small amounts of albumin and other globulin fractions were present. In conditions associated with elevated  $\gamma$  globulin in the serum this globulin was found in higher concentration in the urine.

In contrast to these instances of proteinuria in 21 patients with conditions associated with renal tubular dysfunction (7 with adult Fanconi syndrome, 3 with Wilson's disease, one with idiopathic nephrocalcinosis, one with renal tubular acidosis with nephrocalcinosis, one with congenital galactosemia, 2 with pituitary diabetes insipidus, one with purgative addict [chronic potassium depletion], one with hemolytic disease, one with organic aciduria syndrome, one with acquired renal tubular rickets, one with congenital hypoplastic kidneys with an episode of acute tubular necrosis [recovered] and 1 with cystinuria) the proteinuria was differently constituted. These patients who have more than 15 mg. protein per 100 ml. of urine all showed a distinctive pattern with  $\alpha_2$  globulin in concentration equal to or greater than albumin. Often much  $\beta$  globulin was also present and there may be a relatively high proportion of  $\gamma$  globulin. No relation between this tubular proteinuria and other abnormalities such as aminoaciduria or glycosuria was found. In the patient with galactosemia

the urine protein pattern reverted to normal when the patient ate no galactose. The peculiar pattern found in these patients with renal tubular disorders may have diagnostic importance and also the higher proportion of globulins may bear some relation to the subsequent renal failure in some cases inasmuch as Blackman, Goodwin, and Buell (Bull. Johns Hopkins Hosp. 69: 397, 1941) and Blackman and Davis (J. Clin. Invest. 22: 545, 1943) have suggested that globulinuria is particularly associated with deposition of hyaline material within the tubules and glomeruli and a progression to renal failure, and Lasch (Schweiz. med. Wehnschr. 83: 153, 1953) has correlated globulinuria with a poor prognosis in various forms of nephritis.

DAVID M. KYDD

Nov. 22, 1958.

- \*Gillespie, W. A., Simpson, K., and Tozer, R. C.: Staphylococcal Infection in a Maternity Hospital, p. 1075.
- \*Timbury, M. G., Wilson, T. S., Hutchison, J. G. P., and Govan, A. D. T.: A Staphylococcus Type-80 Epidemic in a Maternity Hospital, p. 1081.
- \*MacGillivray, I., and Buchanan, T. J.: Total Exchangeable Sodium and Potassium in Non-Pregnant Women and in Normal and Pre-Eclamptic Pregnancy, p. 1090.
- \*Embrey, M. P., Garrett, W. J., and Pryer, D. L.: Inhibitory Action of Halothane on Contractility of Human Pregnant Uterus, p. 1093.
- \*Aitken, E. H., Preedy, J. R. K., Eton, B., and Short, R. V.: Oestrogen and Progesterone Levels in Foetal and Maternal Plasma at Parturition, p. 1096.

### Gillespie, Simpson, and Tozer: Staphylococcal Infection in a Maternity Hospital, p. 1075.

In an investigation in the Bristol Maternity Hospital carried out over the course of 21/2 years, cultures were obtained periodically from full-term infants who were kept apart from their mothers except when feeding. Swabs which yielded Staphylococcus aureus were obtained from the umbilicus in 59 per cent of the infants at the age of 2 days, from the groin in 55 per cent, from the nose in 44 per cent, and from the nape of the neck in 27 per cent. The low density of organisms obtained from the last named site suggested that they were present more as contaminants than because of rapid multiplication at this site. The percentage of infants whose nasal cultures yielded staphylococcus steadily increased so that at the time of discharge from the hospital (tenth day) 88 per cent of the infants' noses were infected. This differed from the percentage of positive cultures obtained from the umbilieus and groin which increased to a maximum at about the age of 6 days (about the time the cord remnant became dry and separated) and then declined to somewhat less than 60 per cent at the time of discharge. Cultures of staphylococcus from the nose usually consisted entirely or predominantly of one strain whereas 2 or more strains could often be identified in cultures from the umbilicus and groin. Staphylococci were found to spread more often from the umbilieus to the nose rather than contrariwise. Of the 1,016 staphylococci that were isolated from the infants, 69 per cent were resistant to penicillin and, of these, 18 per cent were insensitive also to streptomycin and 14 per cent to sulfonamide; only one organism was resistant to tetracycline and one other to chloramphenicol. Among 842 infants there were 99 clinical staphylococcus infections (conjunctivitis 38, pemphigus 11, simple pustule 37, paronychia 4, furuncle 4, stye 2, subcutaneous abscess 3). Infants who became staphylococcus carriers in both the nose and umbilicus as early as the second day later developed sepsis more frequently than the other infants. Most staphylococci isolated belonged to phage Groups I and III and these contained 81 per cent of the penicillin-resistant strain. Most Group II organisms were penicillin-sensitive. The staphylococci varied in their ability to cause clinical infections, e.g., all the instances of pemphigus were caused by a Type 71 (Group II) strain. Staphylococci sometimes spread from the nurses' or mothers' noses but once introduced into the nursery they spread from infant to infant without colonizing the nurses' noses.

The disinfection of blankets had no notable effect upon the spread of staphylococci. The use by the nurses of a hand lotion containing one per cent chlorhexidine reduced the number of staphylococci cultured from the nurses' hands but no effect upon the spread of these bacteria among infants could be demonstrated. However, the use of a dusting powder containing hexachlorophene on the umbilicus caused a pronounced reduction in staphylococcal colonization of the umbilicus. Though this needs further evaluation, the introduction of this dusting powder into a nursery was associated with a drop in staphylococcal lesions of the skin from 5.2 per cent to 2 per cent.

DAVID M. KYDD

### Timbury et al.: A Staphylococcus Type-80 Epidemic in a Maternity Hospital, p. 1081.

An epidemic caused by staphylococcus phage Type 80 occurred in a Maternity Hospital with 120 beds divided into 3 separate units. The babies normally stayed beside their mothers' beds but were taken to the nursery attached to each unit for bathing, changing, or if they were noisy. Infants who became ill were transferred to a "sick nursery," of which a pediatrician was in charge. Prior to the epidemic, mild infections due to Staphylococcus aureus were common in the "sick nursery" and phage typing of the organisms that were isolated showed a variety of strains but no Type 80 was found before the epidemic. Type 80 was isolated from a submandibular abscess and during the 6 subsequent weeks, until the hospital was closed, this organism caused 14 of the 18 infections appearing in the "sick nursery." Nine of these 18 infections were serious (abscesses, pneumonia, and one case of osteitis) and all of these serious infections were caused by Type 80. Five of these 9 infants died. In addition, 2 children who were treated in one of the units other than in the "sick nursery" died of Type 80 staphylococcus infections, and one child died a week after being discharged in apparent good health on the eighth day. The responsible organism in the last child, however, was Type 29/7 rather than 80.

After the hospital was closed, 38 per cent of 475 hospital personnel were found to have Staphylococcus aureus in their nasal cultures but only 3 persons harbored the epidemic strain. Of these one was a maid who did not work in the wards, and 2 were nurses. The latter, because they developed boils after the start of the epidemic, were considered to be victims of Type 80 rather than the source. In the fifth week of the epidemic, nasal swabs were taken from 16 healthy babies in the units. When cultured, 13 of these were positive for staphylococcus but only 3 of these were Type 80. When the hospital was closed, various fomites, including dust and furniture, were cultured. Staphylococci were found often enough but Type 80 only once (in a communal blanket).

After discharge, 21 of 99 babies developed an infection but all but one of these were mild. Cultures of 20 lesions yielded only 4 Type 80 organisms and 12 other types of staphylococci (10 penicillin-resistant and 2 penicillin-sensitive). One month after discharge 17 of 18 babies had staphylococci in their noses but only 4 had Type 80. Four months after discharge only 7 of 16 babies harbored staphylococci and of these 2 were Type 80.

After closing, the whole hospital was disinfected by spraying with 10 per cent liquid formaldehyde and the textiles were all sterilized with steam under pressure. The hospital was reopened 18 days later and, although staphylococcus infections have occurred, no Type 80 has been found.

This epidemic, thus, was caused by a virulent Type 80 strain of Staphylococcus aureus. The strain appeared suddenly and spread rapidly despite its low power to colonize in the nasal passages of those who cared for the babies. Also, there was no indication that the strain tended to persist unduly in the noses of children who were known to harbor this type of staphylococcus.

DAVID M. KYDD

### MacGillivray and Buchanan: Total Exchangeable Sodium and Potassium in Non-Pregnant Women and in Normal and Pre-Eclamptic Pregnancy, p. 1090.

With the method of Robinson, Arons, and Solomon (J. Clin. Invest. 34: 134, 1955), the exchangeable sodium and potassium was determined in 24 nonpregnant women and in four

groups of primigravidas (8 with normal pregnancies in the first trimester, 16 with normal pregnancies in the last trimester, 16 with mild pre-eclampsia, and 16 with severe pre-eclampsia). In these five groups the range of values obtained for exchangeable sodium were: nonpregnant 1,645-2,870 mEq. (average 2,265 mEq.), early pregnancy 2,035-2,655 mEq. (average 2,248 mEq.), late pregnancy 2,360-3,515 mEq. (average 3,021 mEq.), mild pre-eclampsia 2,600-3,730 mEq. (average 3,104 mEq.), severe pre-eclampsia 2,425-3,760 mEq. (average 3,126 mEq.). The age, weight, height, and surface area were tried as independent variables and weight was found to be the best single variable. The average results expressed as mEq. Na° per kilogram body weight were: nonpregnant 41.5, early pregnancy 46.2, late pregnancy 48.3, mild pre-eclampsia 44.0, and some pre-eclampsia 43.8. These results were interpreted as showing that in pregnancy the total exchangeable sodium is increased and in late pregnancy is increased still more. In both mild and severe pre-eclampsia, however, the exchangeable sodium is less than in normal pregnancy and no significant difference was found between mild and severe pre-eclampsia.

In these same five groups, the range of values obtained for exchangeable potassium were: nonpregnant 1,770-3,025 mEq. (average 2,370 mEq.), early pregnancy 1,465-2,275 mEq. (average 1,982 mEq.), late pregnancy 2,100-2,950 mEq. (average 2,541 mEq.), mild preeclampsia 1,970-3,450 mEq. (average 2,602 mEq.), severe pre-eclampsia 2,005-2,795 mEq. (average 2,495 mEq.). The average results expressed as mEq. K° per kilogram body weight were: nonpregnant 43.6, early pregnancy 40.4, late pregnancy 40.8, mild pre-eclampsia 36.5, and severe pre-eclampsia 35.1. There was a greater amount of potassium in late pregnancy than in early but no significant difference between the values in late pregnancy and in mild and severe pre-eclampsia. Calculation of the Na/K ratio in pregnancy revealed a relatively greater retention of sodium but the difference between normal late pregnancy and pre-eclampsia was insignificant. No difference in the equilibration time was found for either sodium (6 hours) or potassium (22 hours).

The conclusion was reached that the amount of sodium retained in pre-eclampsia is the same as in normal pregnancy but there is a greater retention of water in pre-eclampsia than in normal pregnancy.

DAVID M. KYDD

### Embrey, Garrett, and Pryer: Inhibitory Action of Halothane on Contractility of Human Pregnant Uterus, p. 1093.

Records of the painless contractions of the uterus in late pregnancy in ten instances and of the contractions in labor in two instances were obtained by means of external tocography. In each instance uterine contractility was clearly inhibited following the induction of Halothane anesthesia with obliteration of both spontaneous and oxytocin-induced contractions. The inhibition was quickly produced and disappeared when consciousness was recovered. The severe slowing of the cardiac rate that has been reported following the administration of Halothane did not occur in these patients who had been pretreated with atropine.

DAVID M. KYDD

### Aitken et al.: Oestrogen and Progesterone Levels in Foetal and Maternal Plasma at Parturition, p. 1096.

Estrone, estradiol-17B, estriol, and progesterone were determined in the maternal and fetal cord plasma in two groups of patients: (A) 7 patients who were delivered by cesarean section for a variety of reasons between the thirty-fifth and forty-first weeks of gestation; (B) 8 patients who were delivered by normal labor between the thirty-eighth and forty-first weeks of gestation. In Group A the mean values obtained in maternal plasma for estrone, estradiol-17B, estriol, and progesterone, respectively, were: 26.6 (S.D. 13.5), 2.8 (S.D. 1.0), 24.4 (S.D. 10.1), and 13.0 (S.D. 5.4) µg per 100 milliliters. In Group B the mean values were 12.0 (S.D. 5.5), 2.2 (S.D. 1.7), 17.8 (S.D. 1.7), and 11.3 (S.D. 4.1). In fetal plasma

(cord blood) the mean values for estrone, estradiol-17B, estriol, and progesterone were, in Group A: 2.15 (S.D. 0.97), 0.66 (S.D. 0.50), 140.8 (S.D. 56.8), and 38.5 (S.D. 15.2) µg per 100 milliliters. In Group B the values obtained were 3.6 (S.D. 1.8), 0.50 (S.D. 0.27), 129.0 (S.D. 43.9), and 46.4 (S.D. 11.2). No significant difference (P = > 0.05) was observed between the mean levels of any of the hormones when the cesarean section samples were compared with those obtained during normal labor. However, there was a highly significant difference (P = < 0.01) between the mean levels in maternal as opposed to fetal plasma. These differences were apparent when the estrogens were determined in maternal and fetal plasma from the same subject. The sex of the infant had no effect on the hormone levels in either the mother or the fetus. The difference in the concentrations in maternal and fetal blood was interpreted as supporting the belief that the fetus is capable of metabolizing rapidly estrone and estradiol-17B but not progesterone. Because of the higher concentrations of estrone and estradiol-17B in maternal plasma, there may be a tendency for these hormones to diffuse toward the fetus, whereas estriol which is presumed destined for excretion and progesterone for metabolism by maternal tissues would tend to diffuse toward the mother. In this study only the total estrogens present were measured and no estimation of "free," "protein-bound," or "conjugated" forms was made. Nevertheless, the data suggest that human parturition is not initiated by any major alteration in plasma estrogen or progesterone concentration.

DAVID M. KYDD

Vol. 1, April 11, 1959.

\*Byrom, F. B., and Pratt, O. E.: Oxytocin and Renal Cortical Necrosis, p. 753.

### Byrom and Pratt: Oxytocin and Renal Cortical Necrosis, p. 753.

Two groups of freshly weaned female albino rats were ovariectomized. Rats in the first group received either 10 mg, of estradiol as an implant or 0.25 mg, estradiol benzoate in oil as a daily injection. In addition, these rats received several daily doses of up to 1 mg, progesterone. Rats in the second group received no estrogens and served as control animals. Ten or more days later some of the rats that had received estrogens were given intravenously small doses (20 to 30 milliunits) of either a synthetic or a natural oxytocin from which the preservative, chlorbutol, had been removed. The kidneys were observed in the living animal by means of a laparotomy, and within a few seconds of the injection evidence of ischemia was seen. After so small a dose the ischemia was relatively short-lived and no structural damage resulted. Other rats received much larger doses of the oxytocin by means of a single subcutaneous injection (4 to 20 or more units per 100 grams body weight). These animals were killed 24 hours after the injection. At the lower level of dose the only histological abnormality is a thin, cloudy eosinophil exudate in the lumen of Bowman's capsule and tubules. When the higher doses are used, the greater part of the cortex is converted into multiple anemic infarcts, usually with hemorrhagic borders. In these areas the tubules are completely necrosed. Some glomeruli may escape damage, others may be completely necrosed. Although patchy tubular dilatation is common, the medulla remains substantially free from necrosis. The renal arteries are usually normal except that some areas of circumscribed medial necrosis of large arteries have been seen.

When injected either subcutaneously or intravenously, the kidneys of the rats that had received no estrogens did not show any abnormalities until an especially concentrated solution of synthetic oxytocin was given intravenously (0.1 ml. of a solution containing 70 units per milliliter). This was followed by gross blanching. Thus, the effect of ovarian hormones on the reactivity of vascular muscle to oxytocin is not a qualitative but rather a quantitative change.

These observations were believed to be logical corollaries of the demonstration by Lloyd (J. Physiol. 141: 37, 1958) that oxytocin assumes vasoconstrictor properties in the presence of ovarian activity. Even though unnaturally large, toxic doses of oxytocin were

used in these experiments, the kidneys of rats that have received estrogens have been shown to be vulnerable to oxytocin and the changes are comparable to those that have been shown previously following the administration of vasopressin. However, although the reactions of the uterine muscle to oxytocin may be increased several hundredfold at full term, there is no direct evidence that vascular muscle is sensitized in normal or abnormal human pregnancy. The newly revealed vasoconstrictor oxytocin must be added to the list of suspect agents in the renal necrosis that occurs in the last third of pregnancy following accidental hemorrhage.

DAVID M. KYDD

April 18, 1959.

Main, R. A., and Paterson, J. R. S.: Postpartum Pancreatitis With Urticaria, p. 813.

May 2, 1959.

Yeates, W. K.: Palliation in Vaginal Urinary Fistulae, p. 916.

### Münchener medizinische Wochenschrift

Vol. 100, Sept. 12, 1958.

Rohde, I.: Aplasia of the Gonads Appearing With Other Malformations, p. 1374.

Sept. 19, 1958.

\*Runge, H., and Hartert, Irene: Experience With Heparin Therapy, Without Laboratory Control, p. 1416.

Krone, H. A.: The Importance to Prenatal Care of Exogenous Causes of Congenital Malformations, p. 1417.

Runge and Hartert: Experience With Heparin Therapy, Without Laboratory Control, p. 1416.

Heparin has been used safely in treating thrombo-embolic diseases and in prophylaxis against them without coagulation tests. Commarin derivatives subject the patient to the danger of hemorrhage unless close laboratory control is used.

WALTER F. TAUBER

Oct. 24, 1958.

Baitsch, H., and Schwarzfischer, F.: Proof of a Pregnancy Lasting 304 Days Post Cohabitation, p. 1653.

Dec. 26, 1958.

Schaetzing, E.: Error of the Climacteric, p. 2027.

### Zentralblatt für Gynäkologie

Vol. 80, Sept. 6, 1958.

Gorys, H. P.: On the Question of Conduct of Labor in Frank Breech Presentation, p. 1417.

Philadelphy, V.: Aschheim-Zondek Pregnancy Test With a Process of Hormone Concentration, p. 1426.

\*Witt, H. J.: Occurrence and Distribution of Anomalies in the Past 55 Years, p. 1432. Geller, H. F., and Reincke, A.: Examination of Unfixed, Unstained Placental Cotyledons and Hofbauer Cells With "Oblique Light Field Illumination," p. 1442.

\*Weisse, R.: Sulfonamide Prophylaxis in Toxoplasmosis-Suspect Pregnant Women, p. 1446.

Kese, G., Menyasz, E., and Negrut, J.: Spontaneous Delivery at Term of a Primigravida With Tuberculosis of the Uterus and Adnexa (Lesions of the Placenta)—Case Report, p. 1450.

### Witt: Occurrence and Distribution of Anomalies in the Past 55 Years, p. 1432.

Among 240,691 births at 4 German universities from 1901 to 1956, there were 2,667 malformations (1.11 per cent). Central nervous system anomalies were found to have a positive correlation with the age of the mother. Except for genitourinary aberrations, in which males predominated by 79 per cent, no sex difference was found. Socioeconomic and geographic variation were not found.

WALTER F. TAUBER

### Weisse: Sulfonamide Prophylaxis in Toxoplasmosis Suspect Pregnant Women, p. 1446.

Sulfonamides were used on 21 pregnant women suspected of toxoplasmosis. In 4 babies there was a positive Savin-Feldman reaction at birth. Three of these became negative. The fourth could not be followed. There was no evidence of toxoplasmosis in any of the other babies.

The author presents this small series as a promising experiment, requiring further-evaluation.

WALTER F. TAUBER

Sept. 13, 1958.

Martius, G,: On Proving the Presence of Rh-antigen in Tissues, p. 1465.

Beric, B.: Lipoma of the Fallopian Tube-Case Report, p. 1468.

Doerner, G., and Hohlweg, W.: Triggering of the "Overproduction Effect" on the Ovary Due to Choriogonadotropin, p. 1471.

Holtorff, J.: On the Fate of Simple Atypical Epithelium of the Portio, p. 1480.

Sept. 20, 1958.

Fikentscher, R.: The Modern Task in the Study of Fertility and the Treatment of Sterility. Opening Address at the First Session of the German Society for the Study of Fertility and Sterility. p. 1497.

Wicke, A.: Resuscitation of a Newborn With Prolapsed Cord in Labor With Absence of Pulse for 10 Minutes—Case Report, p. 1501.

\*Stange, H. H.: Neoplasia in the Presence of Malformation of the Gonads and Their Importance in Therapy, p. 1503.

Aburel, E., Petreseu, V., and Condrea, H.: Comparative Evaluation of Diagnostic Methods in Genital Tuberculosis, p. 1508.

Gerlei, F., Stangl, J.: Triple Dermoid Cyst of the Fallopian Tube, Partly Lined With Gastric Mucus, With Oil Granuloma—Case Report, p. 1513.

## Stange: Neoplasia in the Presence of Malformation of the Gonads and Their Importance in Therapy, p. 1503.

In 26 cases of rudimentary or hypoplastic ovaries, there were 7 patients with neoplasms. Five of the women were 20 years old or younger. Both the high incidence and the age distribution indicate that underdeveloped ovaries predispose to tumor formation. It is, therefore, suggested that hypoplastic ovaries be removed.

WALTER F. TAUBER

Sept. 27, 1958.

Steglich, I., and Christl, G.: Report on the Clinical Investigation of Fetal Phonocardiography, p. 1529.

Walther, L.: Treatment of Carcinoma by Injection of Androgen Into the Tumor—Case Report, p. 1533.

Maurer, J. J., and Reiher, K. H.: On the Metastasizing of Carcinoma of the Cervix—Case Report, p. 1535.

\*Leinzinger, E., and Ribitsch, F.: Eclampsia in the Department of Gynecology of the University of Graz in the Past 30 Years, p. 1543.

- Bilger, S.: On Pathogenesis and Clinical Picture in Dysgerminoma of the Ovary—Case Report, p. 1548.
- Fuhrmann, L., and Grossmann, H.: Pneumoperitoneum Following Attempted Abortion— Case Report, p. 1556.

### Leinzinger and Ribitsch: Eclampsia in the Department of Gynecology of the University of Graz in the Past 30 Years, p. 1543.

Among 56,505 deliveries at the University of Graz between 1925 and 1954, there were 335 cases of eclampsia (0.59 per cent). Of these patients, 74.9 per cent were primigravidas and 25.2 per cent multiparas. Recurrence in subsequent pregnancies occurred in 2 per cent of patients. Eight per cent had twins. There was a maternal mortality of 13.7 per cent. Infant mortality was lower in cases of cesarean section than in medical inductions.

WALTER F. TAUBER

#### Oct. 4, 1958.

- Duesberg, H., and Tiburtius, H.: On Retinal Hemorrhage in the Newborn, p. 1561.
  Schaad, G.: The Utilization of Modern Anesthetic Procedures in Operative Gynecology, p. 1566.
- Tosetti, K., and Gerth, H.: White Blood Cell Count in Erythroblastosis Fetalis, p. 1580.
  \*Sala, H.: Investigation of Carcinogenic Action of Horse Smegma in the Mouse Vagina, p. 1583.
- Kolarova, O., and Malant, M.: Criteria for the Use of Neuroplegic Agents in Potentiated Anesthesia, p. 1587.
- Luft, H.: Evaluation of Maternal Mortality in the Department of Gynecology of Karl Marx Stadt Hospital, p. 1592.
- Petersohn, K. L.: Hodgkin's Disease of the Female Genital Tract—a Case Report, p. 1599.

### Duesberg and Tiburtius: On Retinal Hemorrhage in the Newborn, p. 1561.

Ophthalmoscopy was done on 506 newborn infants. Sixty-seven of these babies (13.2 per cent) had retinal hemorrhage, with boys predominating in the affected group. Two-year follow-up was possible in only 17 infants. They showed no stigmas. However, more intensive practice of funduscopy in the newborn period may lead to clarification of the etiology of strabismus and amblyopia.

WALTER F. TAUBER

### Sala: Investigation of Carcinogenic Action of Horse Smegma in the Mouse Vagina, p. 1583.

No cervical carcinoma was produced in any of 50 mature virgin mice treated with daily smegma douching for one and one half years. Based on these findings, the authors conclude that the lower incidence of carcinoma of the penis and the cervix in ethnic groups practicing circumcision is based on hereditary, rather than postnatal factors.

WALTER F. TAUBER

#### Oct. 11, 1958.

- Noack, H., and Blaschkowski, E.: On the Question of Graphic Tracing of Cervical Contradictions in Labor, p. 1609.
- Klein, F. K.: Vitiligo in Pregnancy-A Case Report, p. 1616.
- Skulj, V.: Intrauterine Chorionepithelioma Due to Tubal Pregnancy—A Case Report, p. 1629.
- Beck, H. U.: Perforation of the Cecum by a Hematocele Following Ruptured Tubal Pregnancy—Case Report, p. 1634.

### Oct. 18, 1958.

Buchbinder, W., and Franz, G.: Ileus in Pregnancy, p. 1641.

Riemann, S.: On the Problem of Anesthesia for Women With Severe Anemia, Particularly in the Presence of Ruptured Fallopian Tube, p. 1648.

\*Staemmler, H. J.: Prednisone Therapy in Chronic Pelvic Inflammatory Disease, p. 1655. Bobek, K., Cepelak, V., and Matejecek, J.: On Laboratory Diagnosis and Butazolidine Treatment of Postpartum Phlebothrombosis, p. 1664.

### Staemmler: Prednisone Therapy in Chronic Pelvic Inflammatory Disease, p. 1655.

Prednisone was used on 150 patients with pelvic inflammatory disease. Each patient received 10 mg, daily for 2 weeks. Half of the patients were continued on 5 mg, daily for another 10 to 14 days. Of 120 patients who had tubo-ovarian changes, a cure was obtained in one third. Half of the patients had considerable subjective and objective improvement. One sixth were refractory. Most of these subsequently proved to have other pathology. Thirty patients had so-called posterior parametritis. Among these, there were no cases of objective improvement but two thirds became asymptomatic.

WALTER F. TAUBER

Nov. 29, 1958.

\*Zenisck, L., and Herout, M.: Testicular Biopsy in Male Infertility, p. 1869.

Oles, H.: Male Pseudohermaphrodite With Complete Feminization—Case Report, p. 1877.

Klees, E.: On Pathogenesis of Eclampsia in Early Pregnancy—Case Report, p. 1882. Szezesniak, A.: On the Problem of Congenital Tuberculosis—Case Report, p. 1889.

### Zenisck and Herout: Testicular Biopsy in Male Infertility, p. 1869.

Testicular biopsy was compared with clinical findings in 100 sterile men. Patients were selected for surgical or urological repair of the excretory ducts on the basis of the biopsies. Histological evidence of absence of spermiogenesis was used to eliminate hopeless cases. Finally, patients were selected in whom there was some hope for improvement of spermiogenesis with conservative treatment.

WALTER F. TAUBER

Dec. 6, 1958.

Schwarz, P.: Pregnancy Following Scheele Operation for Atrophic Urinary Bladder
—Case Report, p. 1901.

Wenig, H.: A Simplified Method for Radiological Evaluation of Competence of the Sphincter of the Urinary Bladder, p. 1906.

Maurer, H. E., Pietschmann, H., and Maurer, H. J.: On the Question of Changes in the Kidneys and Ureters in the Treatment of Neoplasms in the Female Pelvis—Case Report, p. 1910.

Molnar, G.: On the Question of Treatment of Functional Urinary Incontinence With Prolapse of the Uterus, p. 1923.

\*Friedberg, V.: On the Causes of Proteinuria in Toxemia of Pregnancy, p. 1930.

Schwedt, E. W.: Partial Colpocleisis (Döderlein Method) as Therapy for Prolapse and Associated Incontinence, p. 1939.

### Friedberg: On the Causes of Proteinuria in Toxemia of Pregnancy, p. 1930.

Urinary and edema fluid protein were investigated by electrophoresis in an attempt to explain proteinuria in toxemia. No significant qualitative differences were found. Since glomerular filtrate was also quantitatively identical to edema fluid in its protein content, the difference between urine and edema fluid is explained by tubular reabsorption. Proteinuria is thus shown to be due to capillary permeability changes in the glomeruli identical to blood vessel changes throughout the body.

WALTER F. TAUBER



### Correspondence

### ABO Incompatibility

To the Editors:

The two excellent discussions about ABO incompatibility by Dr. Erlandson and Dr. Cole in the Department of Current Opinion of the September issue of the JOURNAL (Vol. 78, No. 3) were very informative. However, there is one statistic frequently quoted that I am unable to believe, and this was repeated by Dr. Erlandson, who states, "In approximately 95 per cent of these cases the blood type of the mother has been Group O." It is true that more cases of ABO hemolytic disease should be anticipated in Group O mothers and one reason for this is that this is the most common blood group. However, ABO heterospecific pregnancy does occur in Group A and Group B mothers. In a series of my own and on a mathematical basis, approximately 35 per cent of all ABO heterospecific pregnancies are found to involve Group A and Group B mothers. Therefore, unless for some unknown reason Group O mothers have a greater capacity to produce erythroblastotic infants, I see no reason why more than 70 per cent of these cases of ABO hemolytic disease should be found in Group O mothers.

TABLE I. ANTICIPATED MATERNAL, PATERNAL, AND FETAL ABO BLOOD GROUP INCOMPATIBILITY

MATERNAL BLOOD GROUP	%	ANTICIPATED PATERNAL BLOOD GROUPS	MATHEMATICS INVOLVED	ANTICIPATED COMPATIBILITY IN 100 PREGNANCIES		ANTICIPATED HETERO- SPECIFIC
				HOMOSPECIFIC	HETERO- SPECIFIC	PREGNANCIES (%)
0	42	42% Group O 53% Group A or B*	$\begin{array}{c} 42 \times 42 \\ 42 \times 53 \end{array}$	18 8	0 14	38
		5% Group AB†	$42 \times 5$	0	2	
Type pregnancies expected in 42 Group O mothers				26	16	
A	39	81% Group O or A	39 × 81	32	0	13
		14% Group B*	$39 \times 14$	1	4	
		5% Group AB†	$39 \times 5$	1	1	
Type pregnancies expected in 39 Group A mothers				34	5	
В	14	56% Group B or O	14 × 56	8	0	29
		39% Group A* 5% Group AB†	$\begin{array}{c} 14 \times 39 \\ 14 \times 5 \end{array}$	2	4	
Type pregnancies expected in 14 Group B mothers				10	4	
AB	5	All compatible		5	0	0
Type pregnancies expected in 100 mothers				75%	25%	

\*Although about 37 per cent of all marriages are ABO heterospecific (this can also be calculated from this table) only about 24 per cent (or approximately 66 per cent of babies born to incompatible parents) of all pregnancies are ABO heterospecific. This is due to heterozygous A or B husbands and to other factors. Therefore, for example, 53 per cent of 42 Group O mothers is 22 and 66 per cent of 22 is approximately 14 heterospecific pregnancies.

†The fact was taken into consideration that one would anticipate that only half of the babies born to A and B mothers when the father is AB would be heterospecific. With O mothers, all.

To go one step further, it can be added that a mother with Group B blood has almost as great a chance of having an ABO heterospecific pregnancy as a Group O mother. This is not true for Group A. Approximately 29 per cent of all babies born to Group B mothers are heterospecific as compared to 38 per cent for Group O mothers. With only 9 percentage points difference, I can see no reason why it is not almost as important to check cord specimens of babies born to Group B mothers as it is in Group O mothers. In the discussion, both Dr. Erlandson and Dr. Cole state that they are checking only blood groups on the cord blood of babies born to Group O mothers. Perhaps the unusual high incidence reported of 95 per cent in Group O mothers may be due to the fact that minor degrees of hemolytic disease are being missed in Group A and Group B mothers because we are just not looking for them.

Table I, based on the reported distribution of blood groups in the U.S.A. white population (Wintrobe), might possibly help to clarify some of the statements made in the previous paragraphs. I personally have no statistics on ABO hemolytic disease. The incidence of ABO heterospecific pregnancy in our area is approximately 25 per cent. Dr. Erlandson reported an incidence of 20 to 25 per cent of all deliveries. Thirty-five per cent of these heterospecific pregnancies are found in Group A or Group B mothers. Much more important, in our area any series of 100 Group B mothers will have about 30 heterospecific pregnancies and any series of 100 Group O mothers will have about 38 heterospecific pregnancies, so the blood group of a baby born to a Group B mother is just about as important as the blood group of a baby born to a Group O mother.

CHRISTOPHER T. REILLY, M.D.

530 N. Maple Ave. Ridgewood, N. J. Sept. 12, 1959

### Reply by Dr. Erlandson

To the Editors:

Dr. Reilly has in a way answered his own question. It is a fact that far fewer cases of ABO incompatibility in which the mother is Group A or B are seen than might be expected on the basis of mathematical calculation. The discrepancy in expected versus actual incidence has led others to speculate, as he has postulated, that for some reason Group O mothers are better able to produce erythroblastotic infants than are Group A or B mothers. For a discussion of this subject, I refer him to the interesting article by Rosenfield.<sup>1</sup>

It has been suggested that there is another blood factor common to A and B but lacking in O. Such a factor would, therefore, produce greater antigenic effect in the heterospecific pregnancies where the mother is Group O. Another suggested explanation is the occurrence of some degree of cross-reactivity between the antibodies for A and B. Thus, an A baby of an O mother would be subject to the effects of anti-A antibody plus cross-reacting anti-B, etc.

It would seem that at the present time there is not a complete answer to the question Dr. Reilly raises, other than that the incidence of ABO incompatibilities is significantly greater among babies of Group O mothers than among infants of Group A or B mothers. We must indeed be aware that disease can occur, although with less frequency, in babies of Group A or B mothers, and we must continue to observe particularly all infants for the appearance of jaundice.

#### Reference

1. Rosenfield, R. E.: Blood 10: 17, 1955.

MARION E. ERLANDSON, M.D.

CORNELL UNIVERSITY MEDICAL COLLEGE ITHACA, N. Y. SEPT. 17, 1959



### American Board of Obstetrics and Gynecology

The Part I Examinations of the American Board of Obstetrics and Gynecology are to be held in various parts of the United States and Canada, on Friday, Jan. 16, 1960, at 2:00 P.M.

Candidates notified of their eligibility to participate in Part I must submit their case abstracts within 30 days of notification of eligibility. No candidate may take the Written Examination unless the case abstracts have been received in the office of the Secretary.

Current Bulletins outlining present requirements may be obtained by writing to the Secretary's office.

ROBERT L. FAULKNER, SECRETARY 2105 ADELBERT ROAD CLEVELAND 6, OHIO

### Correction

In a review of *Le Placenta humain, aspects morphologiques et fonctionnels*, by Professor Jean Snoeck, published in the August, 1959, issue of the JOURNAL, the price is given as \$25.00

Professor Snoeck has informed us that copies may be obtained from Presses Académiques Europeennes, 98 Chausée de Charleroi, Brussels 6, Belgium, for \$16.00, postpaid.

### **INDEX TO VOLUME 78**

### AUTHOR INDEX\*

ACOSTA-SISON, H., The chance of malignancy in a repeated hydatidiform mole, erg, David, Feldman, E. Bos Kaplan, Solomon, And Wa Chun-I, Hyperlipemia and par ADLERSBERG, KAPLAN, SOLOMON, AND WANG, CHUN-I, Hyperlipemia and pancreatitis, hypercholesteremia and coronary artery disease complicating pregnancy, 851

ALDISERT, CAESAR O. (see GRUHN, HUGHES, AND ALDISERT), 1334

AMMERMAN, HARVEY H. (see STEVENS AND AMMERMAN), 104

ANDRESON, PAUL S. (see ARMSTRONG AND ANDRESON), 442

ANDREWS, MASON C., ANDREWS, WILLIAM C., AND STRAUSS, ARNOLD F., Effects of progestin-induced pseudopregnancy on endometriosis: clinical and microscopic studies, 776

ANDREWS, WILLIAM C. (see ANDREWS, ANDREWS, AND STRAUSS), 776

ANTONY, ARTHUR T., The legacy of the past, 1341

ANZIULEWICZ, JOHN A., DICK. HERMAN T WANG

ANZIULEWICZ, JOHN A., DICK, HERMAN J.,
AND CHIARULLI, EUGENE E., Transplacental naphthalene poisoning, 519
ARBEGAST, NEIL R. (see GRAFF, ARBEGAST,
PHILLIPS, HARRIS, AND FRAZIER), 259
ARMSTRONG, CARL L., AND ANDRESON, PAUL S.,
Metallic intrauterine foreign body in
term pregnancy, 442

Metallic intrauterine foreign body in term pregnancy, 442

Ashitaka, Voshio, Shinohara, Koreaki, Taki, Ichiro, Kosai, Masakazu, Hirose, Garo, and Takayama, Katsumi, Cervical pregnancy, 351

Assali, N. S., Dasgupta, K., and Kolin, A., Measurement of uterine blood flow and uterine metabolism. VI. Effects of oxytocic, vasopressor, and vasodepressor drugs on the blood flow to the postpartum uterus in unanesthetized sheep, 313

Averbach, Louis H., A cervical biopsy instrument: introduction of a new trachelotome, 1312

Babcock, Richard J., and Peterson, John H., Relaxim—its effect on electively induced labor, 33

Baden, Warne F., Gran, George, and Bennack, Gene E., The umbilical cord: simplified ligation using new instrument, latex bands, and open-air aftercare, 136

Barnes, Allan C., Common usage, 915

Barno (see Freeman and Barno), 1172

Bartholomew, R. A. (see Fish, Bartholomew, Colvin, Grimes, Lester, and Galloway), 743

BEAUDRY, PIERRE H., AND LANDING, BEN-JAMIN H., Renal maturity of infants of toxemic mothers, 494
BEHERAN, HUGO (see SCARPA, BEHERAN, RAICES, AND BUR), 821
BELTER, LESTER F., AND CAMILO, MARTA, Dem-onstration of cytomegalic inclu-sions in autolyzed fetal tissue, 1243
BENNACK, GENE E. (see BADEN, GRAN, AND BENNACK), 136
BENNETT, RIDGELY (see CLARK AND RIDGELY), 1169

BENNACK), 136
BENNACK), 136
BENNETT, RIDGELY (see CLARK AND RIDGELY), 1169
BENTLEY, WILLIAM G. (see ROTHMAN, BENTLEY, AND FLOYD), 38
BERK, HOWARD (see EISINGER AND BERK), 438
BERNSTINE, J. BERNARD, AND LUDMIR, ABRAHAM, Hemoglobin and hematocrit studies in the newborn with ligated and nonligated umbilical cords, 66

—, AND FRITZ, MARYANN, Bacteriologic studies in ligated and nonligated umbilical cords, 69
BERNSTINE, R. L., LEBLANC, G. A., AND RICHARDSON, J. F., Glant hydronephrosis complicating pregnancy, 431
COMPLICATION OF AND DEPROPHETIS, ROCCO,

ARDSON, J. F., Giant hydronephrosis complicating pregnancy, 431

BEST, WILLIAM G., AND DEPROPHETIS, ROCCO, Fatal gastric fluid aspiration complicating amniotic fluid embolism, 100

BETSON, JOHNNIE R. (see GOLDEN AND BETSON), 890

BIENIARZ, J., The patho-mechanism of late pregnancy toxemia and obstetrical hemorrhages. II. Placental site and venous drainage of the pregnant uterus, 385

BIHL, JOHN H., The effect of pregnancy on hepatolenticular degeneration (Wii-The effect of pregnancy on

ohn H., The effect of pregnancy on hepatolenticular degeneration (Wilson's disease), 1182
OLIVER B., JR. (see McGaughey, Corey, Scoogin, Bobbitt, and Thornton), 844 BOBBITT,

BOBROW, M. LEO (see PAGANO AND BOBROW), 134

JOSEPH (866 CLARK AND BOURKE),

Brandeberry, Keith R. (see Fleming, Brandeberry, and Pearse), 125
Bratvold, Glorie E. (see de Alvarez, Bratvold, Glorie E. (see de Alvarez, Bratvold, And Harding), 375
Breen, J. L. (see Riva, Hatch, and Breen), 1304
Brody Simony Utania

BRODY, SIMON, Uterine procidentia with incarceration, 647
BROOKS, JEAN BAILEY (see BURWELL AND

Ceration, U1.

BROOKS, JEAN BAILEY (866 BURWELL, BROOKS), 772

BRUNS, PAUL (866 PRYSTOWSKY, HELLEGERS, AND BRUNS), 489

BUR, GRATO E. (866 SCARPA, BEHERAN, RAICES, AND BUR), 821

BURNS, BEAURY C., JR. (866 JONES, GOLDBERG, DAVIS, AND BURNS), 1083

BURWELL, JOHN C., JR., AND BROOKS, JEAN BAILEY, Acute appendicitis in pregnancy, 772

<sup>\*</sup>July, pp. 1-234; August, pp. 235-464; September, pp. 465-696; October, pp. 697-928; November, pp. 929-1160; December, pp. 1161-1394.

C

I. A., AND MILLER, HERBERT C., The effects of pregnancy and labor on the respiratory pattern of the newborn infant—subsequent morbidity and mortality, 1005

MARTA (see BELTER AND CAMILO), 1242 CALKINS.

respiratory pattern of the newborn infant—subsequent morbidity and mortality, 1005

Camilo, Marta (see Belter and Camilo), 1243

Carpentier, Peter J., and Potter, Edith L., Nuclear sex and genital malformation in 48 cases of renal agenesis, with especial reference to nonspecific female pseudohermaphroditism, 235

Carr, Martin (see Douglas, Thomas, Carr, Cullen, and Morris), 960

Carrow, Leon A. (see Milligan, Carrow, and Eggers), 599

Carer, Anne C. (see Siegler, Zeichner, Rubenstein, Wallace, and Carter), 369

Casey, E. S. (see Sweeney, Casey, Raheb, and Castellano, James (see Shell, McIntyre, And Castellano), 1219

Chiarulli, Eugene E. (see Anziulewicz, Dick, and Charellano), 1219

Christy, Nicholas P. (see Jailer, Christy, Longson, Wallace, and Gordon), 1

Chun, L., Gong, G., and Roddick, J. W., Jr., The epithelium of the uterine tube and cervix in patients with endometrial carcinoma: a search for estrogenic effect, 174

Clairon, Annell H., and Solomons, Edward, An evaluation of routine culture examinations for Trichomonas vaginalis and Candida, 1314

Clark, John F. J., and Bennett, Ridgely, Superimposed toxemia, abruptio placentae, hypofibrinogenemia, acute renal shutdown, and paralytic ileus complicating a case of prepregnancy hypertension, 1169

—, And Bourke, Joseph, Advanced ectopic pregnancy, 340

Cohen, Melvin R., The role of culdoscopy in infertility, 266

— (see Gold, Soihet, Hankin, and Cohen), 86

Cole, John T., ABO incompatibility, 669 (Clin-

- (see GOLD, SOIHET, HANKIN, AND COHEN),

Cole, John T., ABO incompatibility, 669 (Clinical problems)
Collins, Charles J., The tables turn, 697
Colvin, E. D. (see Fish, Bartholomew, Colvin, Grimes, Lester, and Galloway), 743

CONNOR, A. C., McFADDEN, J. F., HOUSTON, B. J., AND FINN, J. L., Familial congenital complete heart block, 75
COOPERMAN, NORMAN R., Neonatal anemia due to transplacental blood loss, 64
COPIT, PAUL S. (see LASALVIA, COPIT, AND KONDON), 1212
COREY, E. L., McGAUGHEY, HARRY S., JR., AND

KONDON), 1212
COREY, E. L., MCGAUGHEY, HARRY S., JR., AND THORNTON, W. NORMAN, JR., Observations on the spontaneous motility of human uterine muscle in vitro, 20— (see Hall, McGaughey, Corey, AND THORNTON), 27— (see McGaughey, Corpy, School, 27— (see McGaughey, School, 27— (

TON), 27

— (see MCGAUGHEY, COREY, SCOGGIN, BOBBITT, AND THORNTON), 844

CRAWFORD, EDWARD J., SATCOMB bOTTYOIDES, 618

CREADICK, ROBERT N. (see LOCK, DONNELLY, WELLS, FLOWERS, GREENBERG, AND CREADICK), 755

CULLEN, NIALL MICHAEL (see DOUGLAS, THOMAS, CARR, CULLEN, AND MORRIS), 960

D

DARO, AUGUST F., NORA, ERNEST G., Jr., GOLLIN, HARVEY A., AND HOWELL, RICHARD E., Artery ligation in bleed-ing cervical cancer, 197

A, K. (see Assali, Dasgupta, and Kolin), 313 DASGUPTA.

KOLIN), 313

DAVIS, B. A. (see LASH AND DAVIS), 841

DAVIS, HUGH J. (see JONES, GOLDBERG, DAVIS, AND BURNS), 1083

DE ALVAREZ, RUSSELL R., BRATVOLD, GLORIA E., AND HARDING, GEORGE T., The renal handling of sodium and water in normal and toxemic pregancy, 375

DECKER, WAYNE H. (see HADDAD AND DECKER), 1301

DECOSTA. EDWIN J. (see GERBIE, DECOSTA

DECOSTA, EDWIN J. (see GERBIE, DECOSTA, AND REIS), 57 DEPROPHETIS, ROCCO (see BEST AND DEPROPHE-

D'Esopo, D. Anthony, The mechanism of internal rotation and its application to

mairotation, 530

DE SOUSA, LUIZ MELEIRO, AND LASH, ABRAHAM
F., Hemangiopericytoma of the vulva,
295

DEVAUENT, HERBERT J. (see HARTUNG AND DEVAUENT), 1250
DICK, HERMAN J. (see ANZIULEWICZ, DICK, AND CHIARULLI), 519

— (see KARANDY, DICK, DWYER, AND MCKINNON), 96

y, Helen O., and Planas, Mercedes V., A preliminary study on the inci-dence of occult blood in the stools in pregnancy, 864 DICKENS, HELEN O.,

pregnancy, 864
DIDDLE, A. W., SHOLES, D. M., JR., HOLLINGS-WORTH, JANE, AND KINLAW, S., Cervical carcinoma: cancer cells in the circulating blood, 582
DILLON, THOMAS F., Vasopressin as a hemostatic in gynecologic surgery, 1285
DOKO, FUMIO, Histological study of recurrence in adenocarcinoma of the corpus uteri, 180

180

Donnelly, James F. (see Lock, Donnelly, Wells, Flowers, Greenberg, and Creadick), 755

Douglas, Gordon Watkins, Thomas, Lewis, Carr, Martin, Cullen, Niall Michael, and Morris, Robert, Trophoblast in the circulating blood during pregnancy, 960

Dugger, John H. (see Freund, Kegel, and Dugger), 290

DUGGER, JOHN H. (86 DUGGER), 290

DUNN, LEO J., ROBINSON, J. COURTLANDT, AND STEER, CHARLES M., Maternal death following suture of incompetent cervix during pregnancy, 335

DURFEE, RAPHAEL B., The anterior vaginal suspension operation, 628

DWYER, ROBERT P. (see KARANDY, DICK, DWYER, AND MCKINNON), 96

EASTERDAY, CHARLES L., AND REID, DUNCAN E., Inversion of the puerperal uterus managed by the Haultain technique,

ECKERLING, BENJAMIN (see GOLDMAN AND ECKERLING), 1205
EFSTATION, T. D. (see SCHWALENBERG AND EFSTATION), 860

EGGERS, VIRGINIA (see MILLIGAN, CARROW, AND EGGERS), 599

EISINGER, ROBERT P., AND BERK, HOWARD.
Pneumomediastinum and aspiration
pneumonia complicating labor, 438
ENZER, NORBERT (see JACOBSON AND ENZER). ROBERT P., and Berk, Howard, num and aspiration

868

ERLANDSON, MARION E., ABO incompatibility, 667 (Clinical problems) -, ABO incompatibility (reply), 1369 (Cor-

respondence)

ESTRADA, WILLIAM J., HUNDLEY, R. Z., NORRIS,
J. E., AND GREADY, T. G., Pregnancy
complicated by previous bilateral total
adrenalectomy, 1176

FANGER, HERBERT (see Song, Fanger, and Murphy), 1309
FELDMAN, E. BOSSAK (see Adlersberg, Feldman, Kaplan, and Wang), 851
FERGUSON, JAMES HENRY, AND HATTON, ROBERT L., Abruptio placentae and rupture of the marginal sinus of the placenta: some relationships, 947
FETHERSTON, WILLIAM C. (see SCHMITZ, SMITH, AND FETHERSTON), 1048
FIELDS, HARRY, AND NELSON, PHILIP K., Errors of presentation, 539
FINKELSTEIN, RUTH, AND GOLDBERG, RAYMOND B., Evaluation of a new contraceptive cream-jel based on long-term usage, 657

657

FINN, J. L. (see CONNOR, McFADDEN, HOUSTON,

FINN, J. L. (see CONNOR, McFadden, Houston, And Finn), 75

FISH, John S., Bartholomew, R. A., Colvin, E. D., Grimes, W. H., Jr., Lester, W. M., And Galloway, W. H., The relationship of pregnancy weight gain to toxemia, 143

Fleming, Arthur R., Brandeberry, Keith R., and Pearse, Warren H., Introduction of a metric forceps, 125

Flowers, Charles E., Jr., The placental transmission of barbiturates and thiobarbiturates and their pharmacological action on the mother and the infant, 730

— (see Lock, Donnelly, Wells, Flowers, Greenberg, and Creadick), 755

Floyd, William S. (see Rothman, Bentley, And Floyd), 38

Fluhmann, C. Frederic, The glandular structures of the cervix uteri during pregnancy, 990

Foraker, Alvan G. (see Joel and Foraker),

nancy, 990
FORAKER, ALVAN G. (see JOEL AND FORAKER),
1272

Fox, Clifford H. (see Thornton, Fox, and Smith), 1060
Frank, Richard, and Rubovits, Frank E., Repair of incompetent cervix in a case of twin pregnancy, 333
Frazier, Todd M. (see Graff, Arbegast, Phillips, Harris, and Frazier), 259
Freeman, D. W., and Barno, A., Deaths from Asian influenza associated with pregnancy, 1172

Asian influenza associated with pregnancy, 1172

FREUND, DONALD R., KEGEL, EUGENE E., AND DUGGER, JOHN H., Primary malignant melanoma of the vagina, 290

FRITZ, MARYANN (see BERNSTINE, LUDMIR, AND FRITZ), 69

— (see Montgomery, Wise, Lang, Mandle, AND FRITZ), 1227

FULLERTON, RICHARD E. (see LUND, FULLERTON, AND TRISTAN), 706

FULSHER, REMY W., Tubal pregnancy following homolateral salpingectomy, 355

G

GALLOWAY, W. H. (see Fish, Bartholomew, Colvin, Grimes, Lester, and Gallo-WAY), 743

GAMBLE, CLARENCE J. (see STONE AND GAMBLE).

GAMBLE, CLARENCE J. (see STONE AND GAMBLE), 279
GARDNER, G. H., GRENNE, R. R., AND RANNEY, BROOKS, The histogenesis of endometriosis, 445 (Re-evaluation)
GARRY, JOHN, Spontaneous detachment of the cervix during labor, 1221
GAVIAN, NATALIE G. (see SMITH, SMITH, AND GAVIAN), 1028
GERBIE, ALBERT B., DECOSTA, EDWIN J., AND REIS, RALPH A., Fetal hemoglobin as an index of maturity, 57
GERGELY, ELMER, AND MASON, DANIEL J., Pregnancy in a noncommunicating rudimentary horn, 1202
GIBSON, GEORGE B., The repair of genital prolapse, 1275
GOLD, JAY J., SOIHET, SAMUEL, HANKIN, HENRY, AND COHEN, MELVIN R., Hormone therapy to control postpartum breast manifestations, 86

Goldberg, Benjamin (see Jones, Goldberg, Davis, and Burns), 1083
Goldberg, Raymond B. (see Finkelstein And Goldberg), 657
Golden, Max L., and Betson, Johnnie R., Spontaneous rupture of the gravid uterus due to placenta accreta, 890
Goldman, Jack A., and Eckerling, Benjamin, An unusual case of rupture of a pregnant rudimentary horn of a bicornuate uterus, 1205
Gollin, Harvey A. (see Daro, Nora, Gollin, And Howell), 197
Golub, Leib J., A new exercise for dysmenor-rhea, 152
Gong, G. (see Chun, Gong, and Raddick), 174

Gong, G. (see Chun, Gong, and Raddick), 174

Gordon, W. E. L. (see Jailer, Christy, Longson, Wallace, and Gordon), 1

Graff, Thomas D., Arbegast, Neil R., Phillips, Otto C., Harris, Leroy C., and Frazier, Todd M., Gas embolism; a comparative study of air and carbon dioxide as embolic agents in the systemic venous system, 259

Graham, John B. (see Skjorten and Graham), 593

Gran, George (see Baden, Gran, and Bennack), 136

Gravlee, L. C. (see Wideman, Gravlee, and Jones), 200

Gray, J. D., The problem of spontaneous abor-

Jones), 200
Gray, J. D., The problem of spontaneous abortion. VI. Serum seromucoid, hexose, and hexosamine in spontaneous abortion and rheumatoid arthritis, 322

—. Tupper, Carl, and Rowse, J. A., The problem of spontaneous abortion. VII. Prematurity and spontaneous abortion, 325

Charles Mary Lange (Pleyer, and Gray)

GRAY, MARY JANE (see PLENTL AND GRAY),
472
GREADY, T. G. (see ESTRADA, HUNDLEY, NORRIS, AND GREADY), 1176
GREEN, PAUL, AND RUBIN, LEON, Amenorrhea
as a manifestation of chronic liver

as a manifestation of chronic liver disease, 141
GREENBERG, BERNARD S. (see Lock, Donnelly, Wells, Flowers, Greenberg, and Creadick), 755
GREENE, R. R. (see GARDNER, GREENE, AND RANNEY), 445 (Re-evaluation)
GRIMES, W. H., Jr. (see Fish, Bartholomew, Colvin, Grimes, Lester, and Galloway), 743
GRUHN, John G., Hughes, John C., and Aldisert, Caesar O., Tumors of the peripheral nervous system of gynecologic interest: report of a case of neurilemmoma within the right broad ligament mimicking an ovarian cyst, 1334

2334 EST, PHILLIP (see HOFFMAN GRUNDFEST), 428 GRUNDFEST.

#### H

HADDAD, GEORGE H., AND DECKEE, WAYNE H.,
Superior mesenteric syndrome following pelvic inflammatory disease, 1301
HALL, DAVID G., McGAUGHEY, HARRY S., JR.,
COREY, E. L., AND THORNTON, W.
NORMAN, JR., The effects of magnesium therapy on the duration of labor,
27

HALLENBECK, GEORGE A. (see MALKASIAN, WELCH, AND HALLENBECK), 112
HANKIN, HENRY (see GOLD, SOIHET, HANKIN, AND COHEN), 86

AND COHEN), 86

HARDIN, ROBERT C. (see KEETTEL, KINGSBURY, AND HARDIN), 1324

HARDING, GEORGE T. (see DE ALVAREZ, BRATVOLD, AND HARDING), 375

HARRIS, LEROY C. (see GRAFF, ARBEGAST, PHILLIPS, HARRIS, AND FRAZIER), 259

HARTUNG, WALTER H., JR., AND DEVAUENT, HERBERT J., Preliminary report of an electroplating test of urine for pregnancy, 1250

nancy, 1250

HATCH, R. P. (see RIVA, HATCH, AND BREEN), 1304

HATTON, ROBERT L. (see FERGUSON AND HATTON), 947

HELLEGERS, ANDRE (see PRYSTOWSKY, HELLEGERS, AND BRUNS), 489

HELLMAN, LOUIS M. (see KNAPP AND HELLMAN), 570

HENDRICKS, CHARLES H., AND TUCKER, GARY J.,
The direct effect of hypertonic sodium chloride on spontaneous contractility in human and rat myometrium, 13

HILL, HAROLD H., LEBHERZ, THOMAS B., AND MCMAHON, EDMUND B., SARCOMA botryoides, 621

HILTON, JAMES G., AND JOHNSON, RICHARD F., Changes in blood oxytocinase during parturition, 479

HINKAMP, JOSEPH F., AND SZANTO, PAUL B., Chloroma of the ovary, 812

HIROSE, GORO (see Ashitaka, Shinohara, Taki, Kosai, Hirose, and Taka-yama), 351

TAKI, KOSAI, HIROSE, AND TAKAYAMA), 351

HOFFMAN, DAVID B., AND GRUNDFEST, PHILLIP,
Vaginitis emphysematosa, 428

HOLLINGSWORTH, JANE (see DIDDLE, SHOLES,
HOLLINGSWORTH, AND KINLAW), 582

HON, EDWARD H., The fetal heart rate patterns preceding death in utero, 47

HOUSTON, B. J. (see CONNOR, MCFADDEN,
HOUSTON, AND FINN), 75

HOWARD, FORREST H., The physiologic position
for delivery, 1141 (Re-evaluation)

HOWELL, RICHARD E. (see DARO, NORA, GOLLIN, AND HOWELL), 197

HUGHES, JOHN C. (see GRUHN, HUGHES, AND
ALDISERT), 1334

HUNDLEY, R. Z. (see ESTRADA, HUNDLEY, NORRIS, AND GREADY), 1176

HUNTER, CHARLES A., JR., AND NICHOLAS,
HAROLD J., A Study of vaginal acids,
282

HUSTON, I. WUSON, (see, Newson, AND, MAR

Huston, J. Wilson (see Nelson and Huston), 1298

ISRAEL, S. S. LEON, Dysfunctional bleeding, 672 (Clinical problems)

JACOBSON, FOSTER J., AND ENZER, NORBERT, Hydatidiform mole with "benign" metastasis to lung, 868

JAILER, JOSEPH W.. CHRISTY. NICHOLAS P., LONGSON, DONALD, WALLACE, ELEANOR Z., AND GORDON, W. E. L., Further observations on adrenal cortical function during pregnancy, 1

JAYER CARL T. Excribity after cervical dila-

JAVERT, CARL T., Fertility after cervical dilatation, 974

JEFFCOATE, T. N. A., AND SCOTT, J. S., Toxemia of pregnancy (reply), 690 (Correspondence)

spondence)

JEWETT, JOHN F. (see McKay, Jewett, and Reid), 546

JOEL, ROBERT V., and Foraker, Alvan G., The fate of the corpus albicans: a quantitative approach, 1272

JOHNSON, RICHARD F. (see HILTON AND JOHNSON), 479

JOHNSTON, JAMES W., KERNOLLE, JOHN ROBERT, AND SAUNDERS, CHARLES L., JR., Arrhenoblastoma of the right ovary, 800

Jones, ELLIS, Dysgerminoma of the ovary, 825
Jones, Howard W., Jr., Goldberg, Benjamin,
Davis, Hugh J., and Burns, Beaury
C., Jr., Cellular changes in vaginal
and buccal smears after radiation:
an index of the radiocurability of
carcinoma of the cervix, 1083
Jones, W. N. (see WIDEMAN, GRAVLEE, AND
JONES), 200
JUSTEN, J. W., Meigs' syndrome, 830

KAHANE, ALBERT J., AND MARTIN, FRANCISCO B., Maternal death resulting from acute gastric hemorrhage due to Schistosoma mansoni, 1194
KAISER, IRWIN H., A Robert pelvis, 1208
KAKU, MICHITAKA, AND NAGATA, HIDEKAZU, Hypertensive lineage and toxemia of pregnancy, 399
KAPLAN, SOLOMON (see ADLERSBERG, FELDMAN, KAPLAN, AND WANG), 851
KARANDY, EUGENE J., DICK, HERMAN J., DWYER, ROBERT P., AND MCKINNON, 'HARRY J., Fatal air embolism, 96
KATSH, SEYMOUR, Infertility in female guinea pigs induced by injection of homologous sperm, 276
KAUFMAN, MORTON S. (see WALTERS AND KAUFMAN), 274
KEETTEL, WILLIAM C., KINGSBURY, KENNETH L., AND HARDIN, ROBERT C., A Study of the injection of blood intraperitoneally into women, 1324
KEGEL, EUGENE E. (see FREUND, KEGEL, AND DUGGER), 290
KERNODLE, JOHN ROBERT (see JOHNSTON, KERNODLE, JOHN ROBERT (see JOHNSTON, KERNODLE, AND SAUNDERS), 800
KIEKHOFER, WILLIAM (see PECKHAM AND KIEKHOFER), 1012
— (see PECKHAM AND KIEKHOFER), 1120
KIMBROUGH, ROBERT A., Antepartum hemorrhage, 1161

KIMBROUGH, ROBERT A., Antepartum hemorrhage, 1161
KING, ARTHUR G., Prevention of puerperal breast engorgement with large doses of long-acting estrogen, 80

—, The auctioneer's puff, 214 (Pertinent com-

ments)

KINGSBURY, KENNETH L. (see KEETTEL, KINGS-BURY, AND HARDIN), 1324 KINLAW, S. (see DIDDLE, SHOLES, HOLLINGS-WORTH, AND KINLAW), 582

Kirkland, John A., Abdominal menstrual fistula, 1292 Knapp, Robert C., and Hellman, Louis M., Acute renal failure in pregnancy, 570

KOHL, SCHUYLER G. (see SOLOMONS, KRAMER, STEIN, AND KOHL), 513
KOLIN, A. (see ASSALI, DASGUPTA, AND KOLIN), 313

KONDON, V. E. (866 LASALVIA, COPIT, AND KONDON), 1212
KORMAN, WILLIAM (866 RADMAN AND KOR-

MAN), 604

MAN), 504

(see Wizenberg, Siegel, Korman, and Rosenthal), 405

Kosai, Masakazu (see Ashitaka, Shinohara, Taki, Kosai, Hirose, and Takaya-Ma), 351

Kormanus H. L. Carcinoma of the corms

KOTTMEIER, H. L., Carcinoma of the corpus uteri: diagnosis and therapy, 1127 KRAMER, BENJAMIN (see SOLOMONS, KRAMER, STEIN, AND KOHL), 513

L

LANDING, BENJAMIN H. (see BEAUDRY AND

LANDING, BENJAMIN H. (see BEAUDRY AND LANDING), 494

LANG, WARREN R. (see MONTGOMERY, WISE, LANG, MANDLE, AND FRITZ), 1227

LAPAN, BERNARD, A new agent for the treatment of vaginal candidiasis, 1320

LASALVIA, LUCY A., COPIT, PAUL S., AND KONDON, V. E., Evaluation of paravertebral lumbar sympathetic block in labor 1212

Lash, A. F., AND DAVIS, B. A., Squamous cell carcinoma of the vulva in young women, 841

— (see DE SOUSA AND LASH), 295
LASH, S. R., AND RUBENSTONE, A. I., Adenocarcinoma of the rectovaginal septum probably arising from endometriosis, 299

Laurain, Alan R., and Monroe, Thomas C.,
Mixed mesodermal sarcoma of the
corpus uteri associated with bilateral thecoma, 613
Lebherz, Thomas B. (see Hill, Lebherz,
and McMahon), 621

Lebherz, Thomas B. (see Hill, Lebherz, And McMahon), 621
Leblanc, G. A. (see Bernstine, Leblanc, And Richardson), 431
Lehfeldt, Hans, Willful exposure to unwanted pregnancy (Weup), 661
Lepow, Harold, Choriocarcinoma, 884
Lester, W. M. (see Fish, Bartholomew, Colvin, Grimes, Lester, and Galloway), 743
Levinson, J. (see Winkelstein and Levinson), 420
Linton, Eugene B., and Miller, Emery C., Jr., Serum lactic dehydrogenase in pregnancy, 11
Lock Frank R., Donnelly, James F., Wells,

LINTON, EUGENE B., AND MILLER, EMERY C.,
JR., Serum lactic dehydrogenase in
pregnancy, 11
LOCK, FRANK R., DONNELLY, JAMES F., WELLS,
BRADLEY, FLOWERS, CHARLES E., JR.,
GREENEBERG, BERNARD S., AND CREADICK,
ROBERT N., Perinatal mortality in the
primigravida over 30 years of age, 755
LONGSON, DONALD (see JAILER, CHRISTY,
LONGSON, WALLACE, AND GORDON), 1
LOVETT, B. FRANK, Hemangioma of the uterine
cervix complicating pregnancy, 424
LUDMIR, ABRAHAM (see BERNSTINE AND LUDMIR), 66
— (see BERNSTINE, LUDMIR, AND FRITZ), 69
LUND, CURTIS J., FULLERTON, RICHARD E., AND
TRISTAN, THEODORE A., Cinefluorographic studies of the bladder and
urethra in women, 706

#### M

MACARTHUR, J. L. (see MILLER, WILLIAMS, AND MACARTHUR), 303

MCCALL, MILTON L., The radical vaginal operative approach in the treatment of carcinoma of the cervix, 712

MCELIN, THOMAS W., AND PAALMAN, RUSSELL J., Pessary complications in the management of uterine prolapse. 643

— (see PAALMAN AND MCELIN), 898

MCFADDEN, J. F. (see CONNOR, MCFADDEN, HOUSTON, AND FINN), 75

MCGAUGHEY, HARRY S., JR., COREY, E. L., SCOGGIN, WILLIAM A., BOBBITT, OLIVER B., JR., AND THORNTON, W. NORMAN, JR., Observations on the equilibration of urea between mother and fetus, 844 - (see Corey, McGaughey, and Thornton),

— (see Corey, McGaughey, and Thornton), 20
— (see Hall, McGaughey, Corey, and Thornton), 27
McIntyre, Davis B., Jr. (see Shell, McIntyre, And Castellano), 1219
McKay, Donald G., Jewett, John F., and Reid, Duncan E., Endotoxin shock and the generalized Shwartzman reaction in pregnancy, 546
McKinnon, Harry J. (see Karandy, Dick, Dwyer, and McKinnon), 96
MacLaren, John A., Thornes, R. Douglas, Roby, Charles C., and Reid, Duncan E., An immunologic characteristic of the serum of normal pregnancy, 939
McMahon, Edmund B. (see Hill, Lebherz, and McMahon), 621
Maddi, Frances V. (see Papanicolaou and Maddi), 156
Malkasian, George D., Jr., Welch, John S., and Hallenbeck, George A., Volvulus associated with pregnancy, 112
Mandle, Robert J. (see Montgomer, Wise, Lang, Mandle, and Fritz), 1227
Marcus, M. Bennett, and Quartlebaum, Leon, Recurrent hydatidiform mole complicated by pre-eclampsia, 881
Martin, Francisco B. (see Kahane and

11

cated by pre-eclampsia, 881
Martin, Francisco B. (see Kahane and Martin), 1194
Mason, Daniel J. (see Gergely and Mason),

MAYBERGER, HAROLD W., Adenocarcinoma of thy-roid origin in a benign cystic tera-toma, 817

toma, 817

MERRILL, JAMES A., Ovarian hilus cells, 1258

MEYER, IWAN O., Thrombosis of an ovarian vein varicocele in the postpartum period, 109

MIDDLETON, EDMUND B., AND PERRY, HENRY D., Clinical observations of a synthetic oxytocic with a tokodynamometer,

MILLER, EMERY C., JR. (see LINTON AND MILLER), 11
MILLER, HERBERT C. (see CALKINS AND MILLER),

MILLER, HERBERT C. (886 CALKINS AND MILLER), 1095
MILLER, Jo, WILLIAMS, H. B., AND MACARTHUR, J. L., Hemoglobin changes in labor and the puerperium, 303
MILLES, GEORGE (866 PERL, MILLES, AND

MILLES, GEORGE (see PERL, MILLES, AND SHIMOZATO), 285
MILLIGAN, MILDRED, CARROW, LEON A., AND EGGERS, VIRGINIA, A source of false positives in cytologic interpretation, 599

SUBODH, Extraperitoneal lymphade-nectomy and radical vaginal hyster-ectomy for cancer of the cervix MITRA.

ectomy for cancer of the cervix (Mitra technique), 191

MONROE, THOMAS C. (see LAURAIN AND MONROE), 613

MONTGOMERY, THADDEUS L., WISE, ROBERT I., LANG, WARREN R., MANDLE, ROBERT J., AND FRITZ, MARYANN, A study of staphylococcic colonization of postpartum mothers and newborn infants, 1227

MORRIS, ROBERT (see DOUGLAS, THOMAS, CARR, CULLEN, AND MORRIS), 960
MULLA, NEJDAT, Acute urinary tract infection in pregnancy, 578

MULIA, NEJDAT, Acute urinary tract infection in pregnancy, 578

MUNSICK, ROBERT A., Serotonin and the menopausal flush, 147

MURPHY, CHRISTOPHER J., JR. (see PICOT, THOMPSON, AND MURPHY), 786

MURPHY, THOMAS H. (see SONG, FANGER, AND MURPHY), 1309

NAGATA, HIDEKAZU (see KAKU AND NAGATA),

Nelson, James H., Jr., and Huston, J. Wilson, Lymphocyst formation following pelvic lymphadenectomy, 1298
Nelson, Philip K. (see Fields and Nelson),

NELSO...

NEWTON, MICHAEL

434

NICHOLAS, HAROLD J. (see Ho...

NICHOLAS), 282

NOKES, JOHN M., CLAIBORNE, HERBERT A., JR.,

AND REINGOLD, WILLIAM N., Thecoma

with associated virilization, 722

JAMES F., Carcinoma of the vulva,

(see DARO, NORA, GOL
197

Nora, Ernest G., Jr. (see Daro, Nora, Gol-Lin, and Howell), 197 Norburn, L. M., Presentation and prolapse of the umbilical cord, 1234 Norris, J. E. (see Estrada, Hundley, Norris, and Gready), 1176 Novell, Howard A., The change, 908 (Perti-nant comments)

Novell, Howard A., The nent comments)

#### 0

SIMER, W., Prevention of pregnancy by the Graefenberg ring method, 446 (Re-evaluation) OPPENHEIMER.

OTTAWAY, John P., Hysterectomy, a review of the first five years in a new private hospital, 208 OXORN, HARRY, Shock not related to blood loss, with Escherichia coll septicemia in the obstetric patient, 567

Paalman, Russell J., and McElin, Thomas W., Noninvolution of the placental site, 898

site, 898

— (866 McELIN AND PAALMAN), 643
PAGANO, VITO V., AND BOBROW, M. LEO, A new perineal retractor, 134
PAPANICOLAOU, GEORGE N., AND MADDI, FRANCES V., Further observations on the behavior of human endometrial cells in tissue culture, 156
PAZ-CARRANZA, JULIO, PERLMUTTER, MARTIN, AND PRIGERSON, LOWEL, NOrmal pregnancies in a juvenile hypothyroid patient, 1199
PEARSE, WARREN H., Rubella in pregnancy, 228 (Correspondence)

— (866 FLEMING, BRANDEBERRY, AND PEARSE), 125

PECKHAM,

(866 FLEMING, BRANDEBBRAY, 125
 PECKHAM, BEN, Dysfunctional uterine bleeding, 675
 AND KIEKHOFER, WILLIAM, The movement of tritium-labeled water in the human ovarian follicle, 1012
 AND KIEKHOFER, WILLIAM, The movement of tritium-labeled water in neoplastic cystic structures, 1120
 GEORGE, AND SHIMO-

of tritium-labeled water in neoplastic cystic structures, 1120
PERL, JOHN I., MILLES, GEORGE, AND SHIMOZATO, YUKIO, Vaginal fluid subsequent to panhysterectomy, 285
PERLMUTTER, MARTIN (see PAZ-CARRANZA, PERLMUTTER, AND PRIGERSON), 1199
PERRY, HENRY D. (see MIDDLETON AND PERRY),

Perry, Henry D. (see Middleton and Perry),
42
Peterson, John H. (see Babcock and Peterson), 33
Phillips, Otto C. (see Graff, Arbegast,
Phillips, Harris, and Frazier), 259
Picot, Harrison, Thompson, H. Glenn, and
Murphy, Christopher J., Jr., A consideration of the incompetent cervix,
786
Physicon, Joseph W., Pregnancy and spon-

PILKINGTON, JOSEPH W., Pregnancy and spontaneous delivery following operation for congenital atresia of the vagina,

PLANAS, MERCEDES V. (see DICKENS AND PLANAS), 864
PLENTI, ALBERT A., AND GRAY, MARY JANE. Total body water, sodium space, and total exchangeable sodium in normal and toxemic pregnant women, 472
POST, STANLEY, Hydatidiform mole complicated by eclampsia, 878
POTTER, EDITH L. (see CARPENTIER AND POTTER), 259
PRIGERSON, LOWEL (see PAR CARPENTIER)

POTTER, EDITH L. (See CARPENTIES.
TER.). 259
PRIGERSON, LOWEL (See PAZ-CARRANZA, PERL-MUTTER, AND PRIGERSON), 1199
PRYSTOWSKY, HARRY, Fetal blood studies. XI.
The effect of prophylactic oxygen on the oxygen pressure gradient between the maternal and fetal bloods of the human in normal and abnormal pregnancy, 483

—, HELLEGERS, ANDRE, AND BRUNS, PAUL, Fetal blood studies. XIV. A comparative study of the oxygen dissoperative study of the oxygen dissoperative.

Fetal blood studies. XIV. A com-parative study of the oxygen disso-ciation curve of nonpregnant, preg-nant, and fetal human blood, 489

QUATTLEBAUM, LEON (see MARCUS AND QUATTLEBAUM), 881
QUILLIGAN, EDWARD J., AND TYLER, CARL,
Postural effects on the cardiovascular
status in pregnancy: a comparison
of the lateral and supine postures,
465

RADMAN, H. MELVIN, AND KORMAN, WILLIAM, SARCOMA OF the uterus, 604
RAHEB, E. B. (see SWEENEY, CASEY, RAHEB, AND WELNA), 415
RAICES, ADDLPHO A. (see SCARPA, BEHERAN, RAICES, AND BUR), 821

RAND, ROBERT W. (see STERN AND RAND), 498
RANDALL, L. M., Carcinoma of the breast and
pregnancy, 1354 (Clinical problems)
RANNEY, BROOKS (see GARDNER, GREENE, AND
RANNEY), 445 (Re-evaluation)
REID, DUNCAN E. (see EASTERDAY AND REID),
1224

- (see McKay, Jewett, and Reid), 546 - (see MacLaren, Thornes, Roby, and Reid), 939

REILLY, CHRISTOPHER T., ABO incompatibility, 1368 (Correspondence)
REINGOLD, WILLIAM N. (see Nokes, CLAIBORNE, AND REINGOLD), 722

AND REINGOLD), 722

REIS, RALPH A., Postmenopausal uterine bleeding, 1350 (Clinical problems)

— (see Gerbie, DeCosta, and Reis), 57

RICHARDSON, J. F. (see Bernstine, Leblanc, and Richardson), 431

RIEKSE, JAMES M., Terminal obstetrical anesthesia by means of lumbar sympathetic paravertebral block, 411

DIVA H. HARDER R. P. AND RESEN, I. I.

thetic paravertebral block, 411
RIVA, H. L., HATCH, R. P., AND BREEN, J. L.,
Culdoscopy for infertility, 1304
ROBINSON, J. COURTLANDT (see DUNN, ROBINSON, AND STEER), 335
ROBY, CHARLES C. (see MACLAREN, THORNES,
ROBY, AND REID), 939
RODDICK, J. W., JR. (see CHUN, GONG, AND
RODDICK), 174
ROGERS, T. E., JR., Thrombocytopenia in pregnancy following splenectomy, 806
ROGERS, WAYNE S., Aid for treating Trichomonal infection, 226 (Correspondence) ence)

ROSENTHAL, H. N. (see WIZENBERG, SIEGEL, KORMAN, AND ROSENTHAL), 405
ROTHMAN, EMIL D., BENTLEY, WILLIAM G., AND FLOYD, WILLIAM S., The use of relaxin (Cervilaxin) in accelerating the first stage of labor, 38

ROWSE, J. A. (see GRAY, TUPPER, AND ROWSE), 325

RUBENSTEIN, IRVING (see SIEGLER, ZEICHNER, RUBENSTEIN, WALLACE, AND CARTER), 369

RUBENSTONE NONE, A. I. (see Lash and Ruben-stone), 299

RUBIN, LEON (see GREEN AND RUBIN), 141 RUBOVITS, FRANK E. (see FRANK AND RUBO-VITS), 333

8

Sachs, Henry B., Lactation after hysterectomy in a nulliparous woman, 204
Saunders, Charles L., Jr. (\$ee Johnston, Kernodle, and Saunders), 800
Scarpa, Juan B., Beheran, Hugo, Raices, Adolpho A., and Bur, Grato E., Ovarian tumor, precocious puberty, and adrenal hyperfunction, 821
Scheffey, Lewis C., Albert Holmes Smith: a study in courage, 929
Schmitz, Herrert E. Carcinoma of the breast

Schmitz, Herbert E., Carcinoma of the breast and pregnancy, 1356 (Clinical problems)

—, Smith, Charles J., and Fetherston, William C., Effects of preoperative irradiation on adenocarcinoma of the

uterus, 1048
SCHWALENBERG, R. R.,
The importan SCHWALENBERG, R. R., AND EFSTATION, T. D.,
The importance of cervical mucus
studies in pregnancy, 860
SCOGGIN, WILLIAM A. (see McGAUGHEY, COREY,
SCOGGIN, BOBBITT, AND THORNTON),
\$444

SCOTT, J. S. (see Jeffcoate and Scott), 690 (Correspondence)
SCOTT, ROGER B., AND WHARTON, LAWRENCE R., Jr., The effect of testosterone on experimental endometriosis in rhesus monkeys, 1020
SHELL, F. M., AND NEWTON, MICHAEL, Pheochromocytoma diagnosed at cesarean section for labor obstructed by pelvic neurofibroma, 434

SHELL, JAMES H., JR., McIntyre, Davis B.,
JR., and Castellano, James, Gangrene after use of gamma-dimethylamino-n-propyl phenothiazine hydrochloride (Promazine), 1219
SHIMOZATO, YUKIO (see PERL, MILLES, AND
SHIMOZATO), 285
SHINOHARA, KOREAKI (see ASHITAKA, SHINOHARA, TAKI, KOSAI, HIROSE, AND
TAKATAMA), 351
SHOLES, D. M., JR. (see DIDDLE, SHOLES, HOL-

SHINDHARA, KOREAKI (896 ASHITAKA, SHINOHARA, TAKI, KOSAI, HIROSE, AND
TAKAYAMA), 351
SHOLES, D. M., JR. (896 DIDDLE, SHOLES, HOLLINGSWORTH, AND KINLAW), 582
SIEGEI, I. A. (896 WIZEMBERG, SIEGEL, KORMAN, AND ROSENTHAL), 405
SIEGLER, ALVIN M., ZEICHNER, SIDNEY, RUBENSTEIN, IRVING, WALLACE, ELEANOR Z.,
AND CARTER, ANNE C., EMGORINE
STEIN, IRVING, WALLACE, ELEANOR Z.,
AND CARTER, ANNE C., EMGORINE
SUGIES, FREDRIK, AND GRAHAM, JOHN B.,
Nephrostomy in patients with cancer
of the uterine cervix, 593
SLJORTEN, FREDRIK, AND GRAHAM, JOHN B.,
Nephrostomy in patients with cancer
of the uterine cervix, 593
SLJORTEN, FREDRIK, AND GRAHAM, JOHN B.,
Nephrostomy in patients with cancer
of the uterine cervix, 593
SMATKO, A. J., Smegma in carcinoma of cervix, 226 (Correspondence)
SMITH, CHARLES J. (866 SCHMITZ, SMITH, AND
FETHERSTON), 1048
SMITH, DAVID E. (866 SCHMITZ, SMITH, AND
GAVIAN), 1028
SMITH, GEORGE V. (866 SMITH, SMITH, AND
GAVIAN, NATALIE G., Urinary estrogens in women, 1028
SOIHET, SAMUEL (866 GOLD, SOIHET, HANKIN,
AND COHEN), 86
SOLOMONS, EDWARD, KRAMER, BENJAMIN,
STEIN, WILLIAM W., AND KOHL,
SCHUYLER G., The incidence of ophthalmia neonatorum without prophylaxis, 513
— (866 CLARK AND SOLOMONS), 1314
SOMMERS, SHELDON C., AND THAYER, CHARLES
L., Host factors in carcinoma of the
uterine cervix, 586
SONG, Y. S., FANGER, HERBERT, AND MURPHY,
THOMAS H., Significance of performing dual smear examinations in a
mass screening survey for uterine
cancer, 1309
SOPHAN, JOHN, TOXEMIA of pregnancy, 688
(Cotrespondence)
SOSNOWSKI, J. RICHARD, Factors to be considered in the treatment of ovarian
agenesis, 792
SPEERT, HAROLD, A new name for our specialty? 212 (Pertinent comments)
STEER, WILLIAM W. (866 SOLOMONS, KRAMER,
STEIN, AND KOHL), 513
STEEN, WILLIAM W. (867 SOLOMONS, KRAMER,
STEIN, AND KOHL), 513
STEEN, WILLIAM W. (868 SOLOMONS, KRAMER,
STEIN, AND KOHL), 513
STEEN, WILLIAM W. (868 SOLOMONS, KRAMER,
STEIN, AND KOHL,
AND AMMERMAN, HARVEY
H., Intracranial venous thrombosis
in early pregnancy, 104
STEER, AND EM

T

Takayama, Katsumi (see Ashitaka, Shino-hara, Taki, Kosai, Hirose, and Takayama), 351 Taki, Ichiro (see Ashitaka, Shinohara, Taki, Kosai, Hirose, and Taka-

TAKI, KOSAI, THEOS.,
YAMA), 351
TALLER, HERMAN, The problem of obesity, 1144
(Re-evaluation)
TE LINDE, R. W., Postmenopausal uterine
bleeding, 1347 (Clinical problems)

THAYER, CHARLES L. (see SOMMERS AND THAYER), 586
THOMAS, LEWIS (see DOUGLAS, THOMAS, CARR, CULLEN, AND MORRIS), 960
THOMPSON, H. GLENN (see PICOT, THOMPSON, AND MURPHY), 786
THORNES, R. DOUGLAS (see MACLAREN, THORNES, ROBY, AND REID), 939
THORNTON, W. NORMAN, JR., FOX, CLIFFORD H., AND SMITH, DAVID E., The relationship of the squamocolumnar junction and the endocervical glands to the site of origin of carcinoma of the cervix, 1060
— (see Corey, McGaughey, and Thornton),

— (see Hall, McGaughey, Corby, and Thornton), 27
— (see McGaughey, Corby, Scoggins, Bobbit, and Thornton), 844
TIETZE, CHRISTOPHER, The clinical effectiveness of contraceptive methods, 650
TRISTAN, THEODORE A. (see Lund, Fullerton, and Tristan), 706
Tucker, Gary J. (see Hendricks and Tucker), 13

Tupper, Carl (see Gray, Tupper, and Rowse). TYLER, CARL (see QUILLIGAN AND TYLER), 465

ULFELDER, HOWARD, Radical vulvectomy with bilateral inguinal, femoral, and iliac node resection, 1074

W

MAXWELL N., Ruptured cerebral aneurysm in pregnancy and puerpe-rium, 1189 WACKER,

aneurysm in pregnancy and puerperium, 1189

Wall, Leonard A., Meconium peritonitis with ascites resulting in dystocia, 1247

Wallace, Eleanor Z. (see Jailer, Christy, Longson, Wallace, and Gordon), 1
(see Siecler, Zeichner, Rubenstein, Wallace, and Carter), 369

Wallace, Helen M., Public health aspects of perinatal mortality and morbidity, 522

Walters, Donald, and Kaufman, Morton S., Sterility due to retrograde ejaculation of semen, 274

Wang, Chun-1 (see Adlersberg, Feldman, Kaplan, and Wang), 851

Welch, John S. (see Malkasian, Welch, And Hallenbeck), 112

Wells, Bradley (see Lock, Donnell, Wells, Flowers, Greenberg, and Creadick), 755

Wells, Bradley (see Lock, Donnelly, Wells, Flowers, Greenberg, and Creadick), 755
Welna, J. A. (see Sweeney, Casey, Raheb, and Welna), 415
Wharton, Lawrence R., Two cases of supernumerary ovary and one of accessory ovary, with an analysis of previously reported cases, 1101
Wharton, Lawrence R., Jr. (see Scott and Wharton), 1020
Wideman, G. L., Gravlee, L. C., and Jones, W. N., Arteriovenous aneurysm of the uterine artery and vein following total abdominal hysterectomy, 200
Williams, H. B. (see Miller, Williams, and Macarthur), 303
Winkelstein, L. B., and Levinson, J., Fulminating pre-eclampsia with cesarean section performed under hypnosis. 420
Wise, Robert I. (see Montgomery, Wise, Lang, Mandle, and Fritz), 1227
Wizenberg, M. J., Siegel, I. A., Korman, W., and Rosenthal, H. N., The use of anileridine in labor for the relief of pain, 405

R, SIDNEY (see SIEGLER, ZEICHNER, RUBENSTEIN, WALLACE, AND CARTER), ZEICHNER.

#### SUBJECT INDEX\*

Abdominal menstrual fistula (Kirkland), 1292
pregnancy, endocrine studies in two cases
(Siegler et al.), 369
ABO incompatibility (Erlandson and Cole),
666 (Clinical problems)
(Reilly), 1368 (Correspondence)
(reply) (Erlandson), 1369 (Correspondence)

ence)

Abortion, spontance (Gray, Tupper, and normal (Gray, Tupper, and normal (Gray, Tupper, and normal (Gray, Tupper, and normal (Gray, Tupper), 1161

and rupture of marginal sinus of placenta (Ferguson and Hatton), 947
toxemia, hypofibrinogenemia, acute renal shutdown, and paralytic fleus complicating case of prepregnancy clearly (Clark and Bennett),

Abstracts, 218, 461, 678, 920, 1154, 1359
Acetazolamide (Diamox), decrease in oxygen
consumption associated with prolonged administration (Tenney and
Tschetter), 921 (Abst.)
Acids, vaginal, study of (Hunter and Nicholas), 282

Addison's disease, pregnancy complicated by (Sluder), 808
Adenocarcinoma of corpus uteri, histological study of recurrence (Doko), 180 of the rectovaginal septum, probably arising from endometriosis (Lash and Bubertone), 200

Rubenstone), 299
of thyroid origin in benign cystic teratoma
(Mayberger), 817
of uterus, effects of preoperative irradiation

of uterus, effects of preoperative irradiation on (Schmitz, Smith, and Fetherston), 1048
Adolescent, sex and (Davis), 456 (B. rev.)
Adrenal cortical function and cortisol metabolism in controls and in shock due to infection (Melby and Spink), 924 (Abst.)

to infection (Melby and System 924 (Abst.)
during pregnancy (Jailer et al.), 1
hyperfunction, ovarian tumor, precocious
puberty, and (Scarpa et al.), 821
lesion, diffuse, in Cushing's disease, histologic observations (Ashworth and
Garvey), 678 (Abst.)
tissues from hypertensives, steroid formation by (Cooper et al.), 923

Adrenalectomy, bilateral total, previous, preg-nancy complicated by (Estrada et al.), 1176

al.), 1176 changes in female sexuality after (Waxen-berg, Drellich, and Sutherland), berg, Drelli 683 (Abst.).

Agenesis, ovarian factors in treatment (Sos-nowski), 792 renal, nuclear sex and genital malforma-tion in 48 cases (Carpentier and Potter), 235

Air embolism, fatal (Karandy et al.), 96

paredoxical (Karandy et al.), 96 tudes, high, bone marrow studies in new-born infant at (Reynafarje), 925 Altitudes, (Abst.)

Amenorrhea American

(Abst.)
ea as manifestation of chronic liver
disease (Green and Rubin), 141
Board of Obstetrics and Gynecology, 691, 928, 1160, 1370 (Items)
Cancer Society, 696 (Item)
Gynecological Society, transactions
of eighty-second annual meeting,
929 American American

020

American Gynecological Society, transactions of eighty-second annual meeting, 929

Amniotic fluid embolism, fatal gastric fluid aspiration complicating (Best and deProphetis), 100

Analgesia and anesthesia in labor, 405-423
Anatomy, surgical, Callander's (Anson and Maddock), 456 (B. rev.)

megaloblastic, of pregnancy and puerperium (Giles and Shuttleworth), 684 (Abst.)

neonatal, due to transplacental blood loss (Cooperman), 64

Anesthesia, analgesia and, in labor, 405-423 compatibility of synthetic oxytocin with (Feldman, Forgaard, and Morris), 461 (Abst.)

conduction (paravertebral lumbar sympathetic block) in labor (LaSalvia, Copit, and Kondon), 1212 obstetrical, hypnosis as (Winkelstein and Levinson), 420 terminal, by lumbar sympathetic paravertebral block (Riekse), 411

Aneurysm, arteriovenous, of uterine artery and vein after total abdominal hysterectomy (Wideman, Gravice, and Jones), 200 cerebral, ruptured, in pregnancy and puerperium (Wacker), 1189

Anileridine, use in labor for pain relief (Wizenberg et al.), 405

Anomalies, congenital, hyperemesis gravidarum as possible exogenous cause (Mey), 1159 (Abst.)

occurrence and distribution in past 55 years (Witt), 1364 (Abst.)

Anovulatory sterility, hypercorticalism as cause (Bagnati, Montes, and Zapata), 678 (Abst.)

Antepartum hemorrhage, 1161-1171 (Kimbrough), 1161

Anterior vaginal suspension operation (Durfee), 628

(Kimbrough), 1161 Anterior vaginal suspension operation (Dur-

Anterior vaginal suspension operation (Durfee), 628
Appendicitis, acute, in pregnancy (Burwell and Brooks), 772
Arrhenoblastoma of right ovary (Johnston, Kernodle, and Saunders), 800
Arteriographic study of placental circulation (Borell, Fernstrom, and Westman), 922 (Abst.)
Arteriovenous aneurysm of uterine artery and vein after total abdominal hysterectomy (Wideman, Gravlee, and Jones), 200

<sup>\*</sup>July, pp. 1-234; August, pp. 235-464; September, pp. 465-696; October, pp. 697-928; November, pp. 929-1160; December, pp. 1161-1394.

Artery ligation in bleeding cervical cancer (Daro et al.), 197
and vein, uterine, arteriovenous aneurysm,

a, uterine, arteriovenous aneurysm, following total abdominal hys-terectomy (Wideman, Gravlee, and Jones), 200 rheumatoid, serum seromucoid, hexose, and hexosamine in (Gray), 222

Arthritis,

Ascites, meconium peritonitis with, resulting in dystocia (Wall), 1247
Asian influenza, deaths from, associated with

pregnancy 1172 (Freeman and Barno),

Atresia of vagina, congenital, pregnancy and spontaneous delivery after operation for (Pilkington), 804
Auctioneer's puff (King), 214 (Pertinent comments)
Autoinsemination, pregnancy achieved by (Walters and Kaufman), 274
Autolyzed fetal tissue, cytomegalic inclusions in (Belter and Camilo), 1243
Autoradiography of carcinoma of uterus with radiophosphorus (Stanicek), 225
(Abst.) (Abst.)

B
Bacterial infection, intrauterine, of newborn infant (Benirschke and Clifford), 924 (Abst.)
Bacteriologic studies in ligated and nonligated umbilical cords (Bernstine, Ludmir, and Fritz), 69
Barbiturates and thiobarbiturates and pharmacological action on mother and infant (Flowers), 730
Biopsy, cervical, new trachelotome for (Averbach), 1312
testicular, in male infertility (Zenisck and Herant), 1367 (Abst.)
Birth injuries to spinal cord (Stern and Rand), 498
Bladder and urethra, cinefluorographic studies (Lund, Fullerton, and Tristan), 706
Bleeding cervical cancer, artery ligation for

Bleeding cervical cancer, artery ligation for (Daro et al.), 197 uterine, dysfunctional (Israel and Peckham), 672 (Clinical problems) postmenopausal (Te Linde and Reis), 1347 (Clinical problems) Block, heart, familial congenital complete (Connor et al.), 75 lumbar sympathetic paravertebral, as terminal obstetrical anesthesia (Riekse), 405

405

paravertebral lumbar sympathetic, in labor (LaSalvia, Copit, and Kondon), (LaSalvia, 1212

Blood, circulating, cervical carcinoma cells in (Diddle et al.), 582
fetal studies. Comparison of oxygen dissociation curves of nonpregnant, pregnant and fetal blood (Prystowsky, Hellegers, and Bruns), 489
effect of prophylactic oxygen on oxygen pressure gradient between maternal and fetal bloods (Prystowsky), 483

483

flow and metabolism, uterine measurement (Assali, Dasgupta, and Kolin), 313 intraperitoneal injection, study (Keettel, Kingsbury, and Hardin), 1324 loss, external, blood volume change in relation to, at normal delivery (Robbe and Ström), 218 (Abst.) shock not related to, with Escherichia coli septicemia in obstetric patient (Oxorn), 567 transplacental, neonatal anemia due to (Cooperman), 64 occult, in stools in pregnancy, incidence (Dickens and Planas), 864 oxytocinase, changes, during parturition (Hilton and Johnson), 479 trophoblast in circulating, during pregnancy

trophoblast in circulating, during pregnancy (Douglas et al.), 960

Blcod-Cont'd

volume change in relation to external blood

volume change in relation to external blood loss at normal delivery (Robbe and Ström), 218 (Abst.) Bone marrow studies in newborn infant at high altitudes (Reynafarje), 925 (Abst.)

Book reviews, 455, 917, 1149
Books received, 460, 920, 1153, 1347
Breast cancer, prognosis (Delario), 919 (B.

Breast cancer, prognosis (Delario), 919 (B. rev.)
carcinoma, and pregnancy (Randall and Schmitz), 1353 (Clinical problems) engorgement, puerperal, prevention with large doses of long-acting estrogen (King), 80
manifestations, postpartum, hormone therapy to control (Gold et al.), 86
radiography, gynecologic radiography including (Dalsace and Garcia-Calderon), 456 (B. rev.)
Breathing, abnormal, as prognostic sign in newborn infant (Calkins and Miller), 1005
Broad ligament, neurilemmoma within, mimicking ovarian cyst (Gruhn, Hughes, and Aldisert), 1334
Buccal smears, vaginal and, cellular changes, after radiation: index of radiocurability of cervix carcinoma (Jones et al.), 1083

Callander's surgical anatomy (Anson and Maddock), 456 (B. rev.)
Canadian Society for the Study of Fertility, 696 (Item)
Cancer (see also Carcinoma)
of breast, prognosis (Delario), 919 (B. rev.)
of cervix, bleeding, artery ligation for (Daro et al.), 197
extraperitoneal lymphadenectomy and radical vaginal hysterectomy for

extraperitoneal lymphadenectomy and radical vaginal hysterectomy for (Mitra), 191
patients, changes in serum lactic-acid-dehydrogenase in (Horn and Langrehr), 225 (Abst.)
Candida, Trichomonas vaginalis and, routine culture examinations for (Clark

candida, inchononas vaginalis and, routine culture examinations for (Clark and Solomons), 1314
Candidiasis (thrush), neonatal, effect of nystatin (Mycostatin) on: method of eradicating thrush from hospital nurseries (Harris et al.), 679 (Abst.) vaginal, new agent for treatment (Lapan),

1320

Carbonic anhydrase inhibitor, decrease in oxy gen consumption associated with prolonged administration (Tenney

prolonged administration (Tenney and Tschetter), 921 (Abst.)
Carcinogenic action of horse smegma in mouse vagina, investigation (Sala), 1366 (Abst.)
Carcinoma (see also Adenocarcinoma, Cancer, Choriocarcinoma, Sarcoma) of breast and pregnancy (Randall and Schmitz), 1353 (Clinical problems) cells (cervical) in circulating blood (Diddle et al.), 582 of cervix, 582-603 cancer cells in circulating blood (Diddle et al.), 582 host factors in (Sommers and Thayer), 586

586

nephrostomy in patients with (Skjorten and Graham), 593 radical vaginal operation for (McCall), 712

radiocurability—cellular changes in vag-inal and buccal smears after radia-tion, index (Jones et al.), 1083 relationship of squamocolumnar junction and endocervical glands to site of origin (Thornton, Fox, and Smith).

Carcinoma of cervix-Cont'd

smegma in (Smatko), 226 (Correspond-

carcinoma of cervix—Cont'd
smegma in (Smatko), 226 (Correspondence)
surgery in, 191-199
of corpus uteri, diagnosis and therapy
(Kottmeier), 1127
endometrial, endometrium and, 156-190
diagnosis and therapy (Kottmeier), 1127
of endometrium, epithelium of uterine
ube and cervix in patients with
(Chun, Gong, and Roddick), 174
in young women (Garcia and Constantino), 1155 (Abst.)
of urethra, primary treatment in Department of Gynecology at University
of Würzburg in last 30 years
(Knopp), 1158 (Abst.)
of uterus, autoradiography with radiophosphorus (Stanicek), 225 (Abst.)
dual smear examinations in mass screening for (Song, Fanger, and Murphy),
1309
of vulva, 833-843
(Nolan), 833
squamous cell, in young women (Lash and

(Nolan), 833
squamous cell, in young women (Lash and Davis), 841
Cardiovascular status in pregnancy, postural effects on (Quilligan and Tyler), 465
Cellular changes in vaginal and buccal smears after radiation: index of radiocurability of cervix carcinoma (Jones et al.), 1083
Cerebral aneurysm, ruptured, in pregnancy and puerperium (Wacker), 1189
Cervical biopsy instrument, new trachelotome (Averbach), 1312
dilatation, fertility after (Javert), 974

ervical biopsy instrument, new (Averbach), 1312
dilatation, fertility after (Javert), 974
hostility (Grant), 222 (Abst.)
mucus studies in pregnancy, importance
(Schwalenberg and Efstation), 860
and nasal smears, comparative study (Davis
and Abou-Shabanah), 222 (Abst.)

and nasal smears, comparative study (Davis and Abou-Shabanah), 222 (Abst.) pregnancy (Ashitaka et al.), 351
Cervilaxin, use in accelerating first stage of labor (Rothman, Bentley, and Floyd), 38
Cervix, cancer (see Cancer of cervix; Carcinoma of cervix) carcinoma (see Carcinoma of cervix) epithelium, in patients with endometrial carcinoma (Chun, Gong, and Roddick), 174

glandular structures, during pregnancy (Fluhmann), 990 hemangioma, complicating pregnancy (Lovett), 424 incompetent, 333-339 consideration (Plott Thompson and

incompetent, 33 consideration

incompetent, 333-339
consideration (Picot, Thompson, and Murphy), 786
repair, in case of twin pregnancy (Frank and Rubovits), 333
suture during pregnancy, maternal death following (Dunn, Robinson, and Steer), 325
portio, immediate effects of delivery on, colposcopic study (Zimskind and Lang), 223 (Abst.)
spontaneous detachment, during labor (Garry), 1221
Cesarean section under hypnosis, fulminating pre-eclampsia with (Winkelstein and Levinson), 420
pheochromocytoma diagnosed at (Shell and Newton), 434
to do or not to do (Harris and Nessim), 1156 (Abst.)
Change, the (Novell), 908 (Pertinent comments)

Change, the (Novell), 908 (Pertinent comments)

Chemotaxis as factor in sperm motility (Schwartz, Brooks, and Zinsser), 221 (Abst.)

Child personality, longitudinal studies (Stone and Onque), 1150 (B. rev.)

Chlordantoin for treatment of vaginal candidiasis (Lapan), 1320

Chloroma of ovary (Hinkamp and Szanto), 812

Chlorothiazide, clinical and metabolic study (Assali, Judd, and Mondz), 682 (Abst.)

Chlorothiazide (Diuril), clinical experience with (Dinon, Kim, and Vander

with (Dinon, Kim, and Vander Veer), 920 (Abst.)
influence on water and electrolyte excretion in pre-eclampsia (de Alvarez and O'Lane), 681 (Abst.)
Choriocarcinoma (Lepow), 884
Chorionic tumors, 868-889
Cinefluorographic studies of bladder and urethra (Lund, Fullerton, and Tristan), 706
Circulation, maternal, 444

Circulation, maternal, fetal erythrocytes in (Sipursky et al.), 925 (Abst.) placental, arteriographic study (Borell, Fernstrom, and Westman), 922

(Abst.) uteroplacental (Arts), 918 (B. rev.)

uteroplacental (Arts), 918 (B. rev.)
Cirrhosis, Laennec's, rate of hydrocortisone clearance from plasma in patients with (Christy et al.), 683 (Abst.)
Clinical problems, 666, 1347
Colposcopic study of immediate effects of delivery on portio of uterine cervix (Zimskind and Lang), 223 (Abst.)

(Abst.)
Common usage of English language (Barnes),
915 (Pertinent comments)
Conduction anesthesia (paravertebral lumbar
sympathetic block) in labor (LaSalvia, Copit, and Kondon), 1212
Congress, Second World, on Fertility and Sterility, proceedings (Tesauro, editor), 1151 (B. rev.)
Contraception, 650-665
by Graefenberg ring method (Oppenheimer),
446 (Re-evaluation)

446 (Re-evaluation) Contraceptive cream-jel, new, evaluation, based on long-term usage and Goldberg), 657 methods, clinical effectiveness (Tietze), 650

methods, clinical effectiveness (Tietze), 650
Contractility of myometrium, effect of hypertonic sodium chloride on (Hendricks and Tucker), 13
of pregnant uterus, inhibitory action of Halothane on (Embrey, Garrett, and Pryer), 1362 (Abst.)
Cord, prolapsed, death from, and life from induction of labor, choice (Theobald), 686 (Abst.)
spinal, birth injuries to (Stern and Rand), 498

Cords, umbilical, ligated and nonligated, bac-

teriologic studies in (Bernstine, Ludmir, and Fritz), 69 hemoglobin and hematocrit studies in newborn with (Bernstine and Lud-

newborn with (Bernstine and Ludmir), 66
prolapse, presentation and (Norburn), 1234
simplified ligation with new instrument and
technique (Baden, Gran, and Bennack), 136
Coronary artery disease, hypercholesteremia
and, complicating pregnancy
(Adlersberg), 851
Corpus albicans, fate (Joel and Foraker),
1272
luteum hormone, and 17-betoeterside.

luteum hormone and 17-ketosteroid excretion during labor and puerperium (Cekon and Ehrlich), 464 (Abst.)

uteri, adenocarcinoma, histological study of recurrence (Doko), 180

mixed mesodermal sarcoma of, associated with bilateral thecoma (Laurain and Monroe). 613

Correspondence, 226, 688, 1368

Cortisol metabolism, adrenal cortical function and, in controls and in shock due to infection (Melby and Spink), 924 (Abst.)

Culdoscopy for infertility (Riva, Hatch, and Breen), 1304

role in infertility (Cohen), 266

Culture examinations, routine, for Trichomonas vaginalis and Candida (Clark and

vaginalis and Candida (Clark and Solomons), 1314 tissue, endometrial cells in, behavior (Pa-panicolaou and Maddi), 156

Cushing's disease, diffuse adrenal lesion in, histologic observations (Ashworth and Garvey), 678 (Abst.)

Cyst, ovarian, neurilemmoma within right broad ligament mimicking (Gruhn, Hughes, and Aldisert), 1334

Cystic structures, neoplastic, movement of tritium-labeled water in (Peckham and Kiekhofer), 1120

Cystomas, ovarian (De Santo, Bullock, and Moore), 1154 (Abst.)

Cytologic interpretation, source of false positives in (Milligan, Carrow, and Eggers), 599

Cytomegalic inclusions in autolyzed fetal tissue (Belter and Camilo), 1243

Death, maternal, from acute gastric hemorrhage due to Schistosoma mansoni (Kahane and Martin), 1194
following suture of incompetent cervix during pregnancy (Dunn, Robinson, and Steer), 335
from postmaturity or prolapsed cord and life from induction of labor, choice (Theobald), 686 (Abst.)
in utero, fetal heart rate patterns preceding (Hon), 47

in utero, fetal neart rate patterns preceding (Hon), 47

Deaths from Asian influenza associated with pregnancy (Freeman and Barno), 1172

Defibrination syndrome in pregnancy (Sharp et al.), 685 (Abst.)

Delivery, immediate effects on portio of uterine cervix, colposcopic study (Zimskind and Lang), 223 (Abst.)

normal, blood volume change in relation to external blood loss at (Robbe and Ström), 218 (Abst.)

physiologic position for (Howard), 1141 (Re-evaluation)

spontaneous, after operation for congenital

spontaneous, after operation for congenital atresia of vagina (Pilkington), 804
Department of current opinion, 212, 445, 666, 908, 1141, 1347

Dermoid cyst, adenocarcinoma of thyroid origin in (Mayberger), 817

Descensus and vaginal relaxation, 628-649
Diabetes insipidus and pregnancy (Giardini and Colque), 220 (Abst.)

Diamox, decrease in oxygen consumption associated with prolonged administration (Tenney and Tschetter), 921 (Abst.)

Diatheses, hemorrhagic, in obstetrice (Elec-

Diatheses, hemorrhagic, in obstetrics (Elsner), 927 (Abst.)
Dihydroergotamine, treatment of postoperative and postoartum urinary retention with (Wertsch), 1158 (Abst.)
Dilatation, cervical, fertility after (Javert),

Diseases of vulva (Calandra and Sammarino), 1150 (B. rev.) of women (Roques, Beattie, and Wrigley), 1152 (B. rev.)

Diuril, clinical experience with (Dinon, Kim, and Vander Veer), 920 (Abst.) and metabolic study (Assall, Judd, and Mondz), 682 (Abst.)

Dysfunctional uterine bleeding (Israel and Peckham), 672 (Clinical problems)

Dysgerminoma of ovary associated with teratoma of ovary (Jones), 825

Dysmenorrhea, new exercise for (Golub), 152

Dystocia, meconium peritonitis with ascites resulting in (Wall), 1247

Dystrophia myotonica, nuclear sex chromatin pattern in (Marshall and Thomas), 684 (Abst.)

#### E

Eclampsia in Department of Gynecology of University of Graz in past 30 years (Leinzinger and Ribitsch), 1366

Eclampsia-Cont'd

hydatidiform mole complicated by (Post),

hydatidiform mole completed by 878
liver in (Antia et al.), 1358 (Abst.)
Ectopia cordis in twin (Hurwitt and Lebendiger), 1155 (Abst.)
Ectopic pregnancy (see Pregnancy, ectopic)
Ejaculation, retrograde, of semen, sterility due to (Walters and Kaufman),

Electrocardiography and phonocardiography, fetal, present place in obstetrics for (Smyth and Farrow), 921

(Abst.) excretion, water and, influence of Electrolyte chlorothiazide on, in pre-eclampsia (de Alvarez and O'Lane), 681 (Abst.)

(de Alvarez and O'Lane), 681
(Abst.)

Electroplating test of urine for pregnancy
(Hartung and DeVauent), 1250

Embolism, air, fatal (Karandy et al.), 96
paradoxical (Karandy et al.), 96
amniotic fluid, fatal gastric fluid aspiration
complicating (Best and deProphetis), 100
gas: comparative study of air and carbon
dioxide as intravenous embolic
agents (Graff et al.), 259
and thrombosis in pregnancy 96-111

Endocervical glands, squamocolumnar junction and, relationship to site of
origin of carcinoma of cervix
(Thornton, Fox, and Smith), 1060

Endocrine and functional disorders, 141-155
studies in two cases of term abdominal
pregnancy (Siegler et al.), 369
Endocrinology, clinical (Paschkis, Rakoff, and
Cantarow), 457 (R. rev.)

First International Congress, 928 (Item)
Endometrial carcinoma (see Carcinoma of
endometrium)
cells human in tissue culture (Papanico-

Endometrial carcinoma endometrium)

cells, human, in tissue culture (Papanico-laou and Maddi), 158 Endometriosis, experimental, effect of testos-terone on (Scott and Wharton),

1020

histogenesis (Gardner, Greene, and Ran-ney), 445 (Re-evaluation) Endometrium, carcinoma (see Carcinoma of

and endometrial carcinoma, 156-190
Endosalpinx, metabolism in vitro (Mastroianni, Winternitz, and Lowi), 461

anni, Winternitz, and Lowi), 461
(Abst.)

Endotoxin shock and generalized Shwartzman reaction in pregnancy (McKay, Jewett, and Reid), 546

English language, common usage (Barnes), 915 (Pertinent comments)

Engorgement, breast, puerperal, prevention with large doses of long-acting estrogen (King), 80

Epidemic, staphylococcus type 80, in maternity hospital (Timbury et al.), 136 (Abst.)

Epithelium of uterine tube and cervix in

of uterine tube and cervix in patients with endometrial carci-noma (Chun, Gong, and Roddick). Epithelium 174

Eponymy, essays in—obstetric and gynecologic milestones (Speert), 455 (B. rev.)
Equilibration of urea between mother and fetus (McGaughey et al.), 844
Erythroblastosis, clinical and serological evaluation of low antibody titers in mother in reference to development (Schaumkell), 225 (Abst.)

mother in reference to development (Schaumkell), 225 (Abst.)

Erythrocytes, fetal, in maternal circulation (Zipursky et al.), 925 (Abst.)

Escherichia coli bacteremia, endotoxin shock and, in pregnancy (McKay, Jewett, and Reid), 565

septicemia, shock not related to blood loss with, in obstetric patient (Oxorn), 567

Estrogen long-acting, prevention of puerperal

Estrogen, long-acting, prevention of puerperal breast engorgement with large doses (King), 80

Estrogen-Cont'd

Estrogen—Cont'd

and progesterone levels in fetal and maternal plasma at parturition (Aitken et al.), 1362 (Abst.)

Estrogenic effect in epithelium of uterine tube and cervix in association with endometrial carcinoma (Chun, Gong, and Roddick), 174

Estrogens, urinary, in women (Smith, Smith, and Gavian), 1028

Exercise, new, for dysmenorrhea (Golub), 152

Extraperitoneal lymphadenectomy and radical vaginal hysterectomy for cancer of cervix (Mitra), 191

F

tube and cervix, epithelium, in patients with endometrial carci-noma (Chun, Gong, and Roddick), Fallopian

itives in cytologic interpretation source (Milligan, Carrow, and positives and Eggers)

Familial Female

congenital complete heart block (Connor et al.), 75
pseudohermaphroditism, nonspecific, genital malformation with (Carpentier and Potter), 235
inguinal, and iliac node resection, radical vulvectomy with (Ulfelder), 1074
after Femoral.

Fertility after cervical dilatation (Javert),

and Sterility, Second World Congress, pro-ceedings (Tesauro, editor), 1151 (B. rev.)

Fetal blood studies. Comparison of oxygen

blood studies. Comparison of oxygen dissociation curves of nonpregnant, pregnant, and fetal blood (Prystow-sky, Hellegers, and Bruns), 489 effect of prophylactic oxygen on oxy-gen pressure gradient between ma-ternal and fetal bloods (Prystow-sky), 483

sky), 483 distress, fetal heart rate patterns in (Hon),

distress, fetal heart rate patterns in (Hon),
47
erythrocytes in maternal circulation (Zipursky et al.), 925 (Abst.)
heart rate patterns preceding death in utero (Hon), 47
hemoglobin as index of maturity (Gerbie, DeCosta, and Reis), 57
phonocardiography and electrocardiography, present place in obstetrics for (Smyth and Farrow), 921 (Abst.) thyroid function and development, effect of maternal thyroid function on (Carret al.), 682 (Abst.) tissue, autolyzed, cytomegalic inclusions in (Belter and Camilo), 1243
Fetomaternal leukocyte incompatibility (Payne and Rolfs), 923 (Abst.)
Fetus, mother and equilibration of urea between (McGaughey et al.), 844
and newborn, 47-79, 483-529
First International Congress of Endocrinology, 928 (Item)

928 (Item) abdominal menstrual Fistula,

(Kirkland), 1292

vesicovaginal (Schneiderman and Stream), 1155 (Abst.) Fistulas, vesicovaginal, follow-up (Wenig), 1158 (Abst.) Flush, menopausal, serotonin and (Munsick),

Follicle, ovarian, movement of tritium-labeled water in (Peckham and Kiekhofer),

1012

Forceps, metric, introduction (Fleming, Brandeberry, and Pearse), 125
Foreign body, metallic intrauterine, in term pregnancy (Armstrong and Andreson), 442
FSH, human pituitary, clinical effect (Gemzell, Diczfalusy, and Tillinger), 682 (Abst.)
Functional disorders, endocrine and, 141-155

Gangrene after intravenous promazine (Shell, McIntyre, and Castellano), 1219
Gas embolism: comparative study of air and carbon dioxide as intravenous embolic agents (Graff et al.), 259
Gastric fluid aspiration, fatal, complicating amniotic fluid embolism (Best and deProphetis), 100
hemorrhage due to Schistosoma mansoni, maternal death from (Kahane and Martin), 1194
Genital malformation, nuclear sex and, with renal agenesis (Carpentier and Potter), 235

Genital malformation, nuclear sex and, with renal agenesis (Carpentier and Potter), 235
prolapse, repair (Gibson), 1275
Glands, endocervical, squamocolumnar junction and, relationship to site of iorigin of carcinoma of cervix (Thornton, Fox, and Smith), 1060
Glandular structures of cervix uteri during pregnancy (Fluhmann), 990
Gonadotrophic hormone, reaction of polycystic ovaries to (Stange and Schaumkell), 225 (Abst.)
Graefenberg ring method, prevention of pregnancy by (Oppenheimer), 446
(Re-evaluation)
Graves' synopsis of surgery (Wakely), 918

Graves' synopsis of surgery (Wakely), 918
(B. rev.)
Gravid uterus, spontaneous rupture, due to

(B. rev.)
Gravid uterus, spontaneous rupture, due to placenta accreta (Golden and Betson), 890
Gynecologic(al) interest, tumors of peripheral nervous system of (Gruhn, Hughes, and Aldisert), 1334
milestones, obstetric and—essays in eponymy (Speert), 455 (B. rev.)
nursing, gynecology and (Miller and Avery), 1151 (B. rev.)
and obstetrical history, 1341
radiography including breast (Dalsace and Garcia-Calderon), 456 (B. rev.)
surgery, vasopressin as hemostatic in (Dillon), 1285

surgery, vasopressin as hemostation), 1285
ynecology and gynecologic nursing (Miller and Avery), 1151 (B. rev.)
obstetrics and, for nurses, handbook (Clyne), 1152 (B. rev.) Gynecology

Halothane, inhibitory action on contractility of human pregnant uterus (Em-brey, Garrett, and Pryer), 1362 (Abst.)

brey, Garrett, and Pryer), 1362

Haultain technique, inversion of puerperal uterus managed by (Easterday and Reld), 1224

Headache, postspinal, in obstetrics (Sweeney et al.), 415

Health, public, aspects of perinatal mortality and morbidity (Wallace), 522

Heart block, familial congenital complete (Connor et al.), 75

disease complicating pregnancy, conservative management (Smith and Gatenby), 679 (Abst.)

rate patterns, fetal, preceding death in utero (Hon), 47

Hemangioma of cervix complicating pregnancy (Lovett), 424

Hemangiopericytoma of vulva (de Sousa and Lash), 295

Hematocrit studies, hemoglobin and, in newborn with ligated and nonligated umbilical cords (Bernstine and Ludmir), 66

Hemoglobin changes in labor and puerperium (Miller, Williams, and Macastian)

Hemoglobin changes in labor and puerperium (Miller, Williams, and Macarthur),

fetal, as index of maturity (Gerbie, De-Costa, and Reis), 57 and hematocrit studies in newborn with ligated and nonligated umbilical cords (Bernstine and Ludmir), 66

Hemorrhage, antepartum, 1161-1171

Hemorrhage, antepartum, 1161-1171
(Kimbrough), 1161
from cervix cancer, artery ligation for
(Daro et al.), 197
gastric, due to Schistosoma mansoni, maternal death from (Kahane and Martin), 1194
retinal, in newborn (Duesberg and Tiburtius), 1166 (Abst.)
Hemorrhagic diatheses in obstetrics (Elsner), 927 (Abst.)
Hemostatic, vasopressin as, in gynecologic surgery (Dillon), 1285
Heparin therapy without laboratory control, experience with (Runge and Hartert), 1364 (Abst.)
Hepatic disease, amenorrhea as manifestation (Green and Rubin), 141

(Green and Rubin), 141

Hepatolenticular degeneration (Wilson's disease), effect of pregnancy on ease), effect (Bihl), 1182

ne, serum, in spontaneous abortion and rheumatoid arthritis (Gray), Hexosamine,

Hexose, serum, in spontaneous abortion and rheumatoid arthritis (Gray), 322
Hilus cells, ovarian (Merrill), 1258
Histogenesis of endometriosis (Gardner, Greene, and Ranney), 445 (Re-

evaluation) adrenal e (Ash-

Histologic observations on diffuse adrena lesion in Cushing's disease (Ash worth and Garvey), 678 (Abst.) Histological study of recurrence in adenocar cinoma of corpus uteri (Doko) (Doko).

History, obstetrical and gynecological (Antony), 1341
Hormone, corpus luteum, and 17-ketosteroid excretion during labor and puerperium (Cekon and Ehrlich), 464 (Abst.)

therapy to control postpartum breast manifestations (Gold et al.), 86
Horn, rudimentary, noncommunicating, pregnancy in (Gergely and Mason),

1202

pregnant, of bicornuate uterus, rupture (Goldman and Eckerling), 1205 pital, maternity, staphylococcal infection

pregnant, of bicornuate uterus, rupture (Goldman and Eckerling), 1205
Hospital, maternity, staphylococcal infection in (Gillespie, Simpson, and Tozer), 1360 (Abst.)
staphylococcus type 80 epidemic in (Timbury et al.), 1361 (Abst.)
nurseries, method of eradicating thrush from (Harris et al.), 679 (Abst.)
Host factors in carcinoma of cervix (Sommers and Thayer), 586
Hydatidiform mole with "benign" metastasis to lung (Jacobson and Enzer), 868 complicated by eclampsia (Post), 878 recurrent, complicated by pre-eclampsia (Marcus and Quattlebaum), 881 repeated, chance of malignancy in (Acosta-Sison), 876
Hydrocortisone clearance from plasma, rate, in pregnant women and patients with Laennec's cirrhosis (Christy et al.), 683 (Abst.)
Hydronephrosis, giant, complicating pregnancy (Bernstine, LeBlanc, and Richardson), 431
17-Hydroxycorticosteroid and pregnanediol excretion during labor and post partum, parallel investigation (Cekon and Ehrlich), 1159 (Abst.)
Hypercholesteremia and coronary artery disease complicating pregnancy (Adst.)

(Cekon and Ehrlich), 1159 (Abst.)

Hypercholesteremia and coronary artery disease complicating pregnancy (Adlersberg et al.), 851

Hypercorticalism as cause of anovulatory sterility (Bagnati, Montes, and Zapata), 678 (Abst.)

Hyperemesis gravidarum as possible exogenous cause of congenital anomalies (Mey), 1159 (Abst.)

Hyperfunction, adrenal, ovarian tumor, precocious puberty and (Scarpa et al.), 821

Hyperlipemia and pancreatitis, hypercholesteremia and coronary artery disease complicating pregnancy (Adlersberg et al.), 851
Hypertension, nontoxemic, in pregnancy, symposium (Morris and Brown), 458 (B. rev.)
prepregnancy, case, toxemia, abruptio placentae, hypofibrinogenemia, acute renal shutdown, and paralytic ileus complicating (Clark and Bennett), 1169 1169

Hypertensive lineage and toxemia of preg-nancy (Kaku and Nagata), 399 Hypertensives, steroid formation by adrenal tissues from (Cooper et al.), 923 (Abst.)

Hypnosis, cessrean section performed under, fulminating pre-eclampsia with (Winkelstein and Levinson), 420
Hypofibrinogenemia, toxemia, abruptio placentae, acute renal shutdown, and paralytic lieus complicating case of prepregnancy hypertension (Clark and Bennett), 1169
Hypothysoid patient juvenile normal pressure.

and Bennett), 1169

Hypothyroid patient, juvenile, normal pregnancies in (Paz-Carranza, Perlmutter, and Prigerson), 1199

Hysterectomy, complications, 200-211
lactation after, in nulliparous woman (Sachs), 204
review of five years in new private hospital (Ottaway), 208
total abdominal, arteriovenous aneurysm of uterine artery and vein following (Wideman, Gravlee, and Jones), 200 200

vaginal, radical, extraperitoneal lymphade-nectomy and, for cervix cancer (Mitra), 191

Ileus, paralytic, toxemia, abruptio placentae, hypofibrinogenemia, acute renal shutdown and, complicating case of prepregnancy hypertension (Clark and Benne:t), 1169

Iliac, inguinal, and femoral node resection, radical vulvectomy with (Ulfelder), 1074

1074
Immunologic characteristic of serum of normal pregnancy (MacLaren et al.), 939
Incarceration, uterine procidentia with (Brody), 647
Inclusions, cytomegalic, in autolyzed fetal tissue (Belter and Camilo), 1243
Incompatibility, ABO (Erlandson and Cole), 666 (Clinical problems)
(Reilly), 1368 (Correspondence) (reply) (Erlandson), 1369 (Correspondence) ence)

ence)

ence)
leukocyte, fetomaternal (Payne and Rolfs),
923 (Abst.)
Incompetent cervix, consideration (Picot,
Thompson, and Murphy), 786
repair, in case of twin pregnancy (Frank
and Rubovits), 333
suture during pregnancy, maternal death
following (Dunn, Robinson, and
Steer), 335
Incontinence, stress, anterior vaginal suspension operation in (Durfee), 628
urinary, cinefluorographic studies (Lund,
Fullerton, and Tristan), 706
Induction of labor (see Labor, induction)
Infection, bacterial, intrauterine, of newborn
infant (Benirschke and Clifford),
924 (Abst.)
urinary tract, acute, in pregnancy (Mulla),
578
Infections, stanbylgococie, in mothers and new

Infections, staphylococcic, in mothers and new-born infants (Montgomery et al.), 1227 259-278

culdoscopy for (Riva, Hatch, and Breen),

Infertility-Cont'd

Infertility—Cont'd
in female guinea pigs induced by injection
of homologous sperm (Katsh), 276
female, lyothyronine therapy in (Hassler),
463 (Abst.)
male, l-triiodothyronine in, clinical experience with (Taymor and Selenkow),
463 (Abst.)
testicular biopsy in (Zenisck and Herant),
1367 (Abst.)
role of cuidoscopy in (Cohen), 266
Inflammatory disease, pelvic, superior mesenteric syndrome after (Haddad and
Decker), 1301
Influenza, Asian, deaths from, associated with
pregnancy (Freeman and Barno),
1172

1172

femoral, and iliac node resection, radical vulvectomy with (Ulfelder), 1074 Inguinal, femoral,

Injuries, birth, to spinal cord (Stern and Rand), 498
Instrument, new, for ligation of umbilical cord (Baden, Gran, and Bennack), 136

136
Instruments, new, 125-140
Insufflation, uterotubal, effects of light on (Polishuk), 223 (Abst.)
Internal rotation, mechanism, and application to malrotation (D'Esopo), 530
International Society of Geographical Pathology, 1160 (Item)
Intracranial venous thrombosis in early pregnancy (Stevens and Ammerman), 104

104 Intraperitoneal injection of blood, study (Keettel, Kingsbury, and Hardin),

1324

Intrauterine foreign body in term pregnancy
(Armstrong and Andreson), 442
Inversion of puerperal uterus managed by
Haultain technique (Easterday and
Reid), 1224
Irradiation preparative effects on adopters

Irradiation, preoperative, effects on adenocar-choma of the uterus (Schmitz, Smith, and Fetherston), 1048

Items, 229, 691, 928, 1160, 1370

Jaundice, unexplained, in newborn, relation-ship of vitamin K to (Biskind and Herman), 1157 (Abst.)

Juvenile hypothyroid patient, normal preg-nancies in (Paz-Carranza, Perlmut-ter, and Prigerson), 1199

roid excretion during labor and puerperium, corpus luteum hormone and (Cekon and Ehrlich), 464 17-Ketosteroid excretion (Abst.)

L

abor, analgesia and anesthesia in. 405-423
anileridine for pain relief in (Wizenberg
et al.), 405
complications, 1221-1249
duration, effects of magnesium therapy on
(Hall et al.), 27
first stage, use of relaxin in accelerating
(Rothman, Bentley, and Floyd), 33
induced, effect of relaxin on (Babcock and
Peterson), 33
induction, life from, and death from post-

Peterson), 33
induction, life from, and death from postmaturity or prolapsed cord, choice
(Theobald), 686 (Abst.)
management, 530-545
normal and abnormal, human parturition
(Miller, Evans, and Haas), 455
(B. rev.)
obstructed by neurofibroma, pheochromocytoma diagnosed at cesarean section
for (Shell and Newton), 434

Labor-Cont'd

paravertebral lumbar sympathetic block in (LaSalvia, Copit, and Kondon), 1212

physiology and therapy, 13-46 pneumomediastinum and aspiration pneu-monia complicating (Eisinger and Berk), 438

Berk), 438
and post partum, pregnanediol and 17hydroxycorticosteroid excretion during, parallel investigation (Cekon
and Ehrlich), 1159 (Abst.)
pregnancy and, complications, 424-444
effects on respiratory pattern of newborn
infant (Calkins and Miller), 1005
and puerperium, corpus luteum hormone and
17-ketosteroid excretion during
(Cekon and Ehrlich), 464 (Abst.)
hemoglobin changes in (Miller, Williams,
and Macarthur), 303
spontaneous detachment of cervix during
(Garry), 1221
actation, 80-95

actation, 80-95 after hysterectomy (Sachs), 204 in nulliparous woman

Lactic dehydrogenase, serum, in pregnancy (Linton and Miller), 11

(Linton and Miller), 11

Lactic-acid-dehydrogenase, serum, changes, in cancer patients (Horn and Langrehr), 225 (Abst.)

Laennec's cirrhosis, rate of hydrocortisone clearance from plasma in patients with (Christy et al.), 683 (Abst.)

Lateral and supine postures, comparison of effects on cardiovascular status in pregnancy (Quilligan and Tyler), 465

Latex bands use in ligation of umbilical cord

Latex bands, use in ligation of umbilical cord (Baden, Gran, and Bennack), 136 Legacy of past (Antony), 1341

Legacy of past (Antony), 1341

Leukemia, acute granulocytic, in pregnancy
(Rothberg, Conrad, and Cowley),
921 (Abst.)

Leukocyte incompatibility, fetomaternal
(Payne and Rolfs), 923 (Abst.)

Ligation, artery, for bleeding cervical cancer
(Daro et al.), 197

of umbilical cord, simplified, with new instrument and technique (Baden, Gran, and Bennack), 136

Light, effects on uterotubal insufflation
(Polishuk), 223 (Abst.)

Liver disease, amenorrhea as manifestation
(Green and Rubin), 141

in normal pregnancy, pre-eclampsia, and eclampsia (Antia et al.), 1358
(Abst.)

(Abst.)

L-triiodothyronine in male infertility, clinical experience with (Taymor and Selenkow), 463 (Abst.) Lumbar sympathetic block, paravertebral, in labor (LaSalvia, Copit, and Kon-don), 1212

paravertebral block as terminal obstetrical anesthesia (Riekse), 411

Lung, "benign" metastasis of hydatidiform mole to (Jacobson and Enzer), 868

Lymphadenectomy, extraperitoneal and radical vaginal hysterectomy for cancer of cervix (Mitra), 191

pelvic lymphocyst formation after (Nelson and Huston), 1298

Lymphocyst formation following pelvic lymphadenectomy (Nelson and Huston), 1298

Lyothyronine therapy in female infontility

ne therapy in female infertility (Hassler), 463 (Abst.) Lyothyronine

M

Magnesium therapy, effects on duration of labor (Hall et al.), 27

Malformation, genital, nuclear sex and, with renal agenesis (Carpentier and Potter), 235 with (Carpent), 1365

of ovaries, neoplasia with (Stange), 1365 (Abst.) Malformations of uterus and pregnancy, 1202-1211

Malignancy in repeated hydatidiform mole, chance of (Acosta-Sison), 876
Malrotation, mechanism of internal rotation and application to (D'Esopo), 530
Marginal sinus of placenta, rupture, and abruptio placentae (Ferguson and Hatton), 947
Marriage of sterile and once sterile female, sexual tones in (Rommer and Rommer), 221 (Abst.)
Maternal circulation, fetal erythrocytes in (Zipursky et al.), 925 (Abst.)
death from acute gastric hemorrhage due to Schistosoma mansoni (Kahane and Martin), 1194
following suture of incompetent cervix during pregnancy (Dunn, Robinson, and Steer), 335
and fetal bloods, effect of prophylactic oxygen on the oxygen pressure gradient between (Prystowsky), 482
Maternity, guide to prospective motherhood (Goodrich), 918 (B. rev.)
hospital, staphylococcal infection in (Gillespie, Simpson, and Tozer), 1360 (Abst.)

pie, Si (Abst.)

staphylococcus type 80 epidemic in (Timbury et al.), 136 (Abst.)

Maturity, fetal hemoglobin as index (Gerbie, DeCosta, and Reis), 57

Meconium peritonitis with ascites resulting in dystocia (Wall), 1247

Megaloblastic anemia of pregnancy and puerperium (Giles and Shuttleworth), 684 (Abst.)

Meigs' syndrome (Justen), 830

Melanoma, primary malignant, of vagina (Freund, Kegel, and Dugger), 290

Menopausal flush, serotonin and (Munsick), 147

Menopause (Novell), 908 (Pertinent comments)

Menopause (Novell), 908 (Pertinent comments)
Menstrual fistula, abdominal (Kirkland), 1292
Menstruation and systemic disease (Rogers), 926 (Abst.)
Mesenteric syndrome, superior, after pelvic inflammatory disease (Haddad and Decker), 1301

Metabolism of human endosalpinx in vitro
(Mastrojanni, Winternitz and
Lowi). 460 (Abst.)
uterine, blood flow and, measurement (Assali,
Dasgupta, and Kolin), 313

Metallic intrauterine foreign body in term
pregnancy (Armstrong and Andreson). 442

pregnancy (Armstrong and Andreson), 442
Metastasis, "benign," of hydatidiform mole to lung (Jacobson and Enzer), 868
Metastatic trophoblastic tumors of testis, therapy with Methotrexate (Bruckner), 921 (Abst.)
Methotrexate therapy of metastatic trophoblastic tumors of testis (Bruckner), 921 (Abst.)

Metric forceps, introduction (Fleming, Brandeberry, and Pearse). 125
Mitra technique of extraperitoneal lymphadenectomy and radical vaginal enectomy and radical vaginal hysterectomy for cervix cancer

hysterectomy for cervix cancer (Mitra), 191
Mole, hydatidiform, with "benign" metastasis to lung (Jacobson and Enzer), 868 complicated by eclampsia (Post), 878 recurrent. complicated by pre-eclampsia (Marcus and Quattlebaum), 881 repeated, chance of malignancy in (Acosta-Sign), 876

Sison), 876
Morbidity and mortality associated with respiratory pattern of newborn infant (Calkins and Miller), 1005
perinatal, public health aspects (Wallace), 522
Mortalian

Mortality, perinatal, in North Carolina Memorial Hospital (Flowers, Weinel, and Kirkland), 1157 (Abst.) public health aspects (Wallace), 522 in primigravida over 30 years of age (Lock et al.), 755

Mother and fetus, equilibration of urea between (McGaughey et al.), 844

Motherhood, prospective, guide to (Goodrich),

Motherhood, prospective, guide to (Goodrich),
918 (B. rev.)
Mothers, postpartum staphylococcic infections
(Montgomery et al.), 1227
Motility, spontaneous, of uterine muscle in
vitro (Corey, McGaughey, and
Thornton), 20
Mucus studies, cervical, in pregnancy, importance (Schwalenberg and Efstation), 860
Muscle, uterine, spontaneous motility in vitro
(Corey, McGaughey, and Thornton),
20

20

Mycostatin, effect on neonatal candidiasis (thrush) (Harris et al.), 679 (Abst.)

Myometrium, contractility, effect of hyper-tonic sodium chloride on (Hendricks and Tucker), 13

Name, new, for our specialty? (Speert), 212 (Pertinent comments)

poisoning, tra lowicz, Dick, transplacental (An-Naphthalene ziulewicz, 519 and Chiarulli).

Nasal smears in women, and cervical, com-parative study (Davis and Abou-Shabanah), 222 (Abst.)

renal cortical, oxytocin and (Byrom and Pratt), 1363 (Abst.) anemia due to transplacental blood loss (Cooperman), 64
with malformation of gonads Necrosis, Neonatal

Neoplasia

Neoplasia with malformation of gonads (Stange), 1365 (Abst.)

Neoplastic cystic structures, movement of tritium-labeled water in (Peckham and Kiekhofer), 1120

Nephrostomy in patients with cervix cancer (Skjorten and Graham), 593

Nervous system, peripheral, tumors of gynecologic interest (Gruhn, Hughes, and Aldisert), 1334

Neurilemmoma within right broad ligament

Nervous system, peripheral, tumors of gynecologic interest (Gruhn, Hughes, and Aldisert), 1334

Neurilemmoma within right broad ligament mimicking ovarian cyst (Gruhn, Hughes, and Aldisert), 1334

Neurofibroma, labor obstructed by, pheochromocytoma diagnosed at cesarean section for (Shell and Newton), 434

Newborn, fetus and, 47-79, 483-529
infant, bone marrow studies at high altitudes (Reynafarje), 925 (Abst.) effects of pregnancy and labor on respiratory pattern (Calkins and Miller), 1005
evaluation—second report (Apgar et al.), 681 (Abst.) intrauterine bacterial infection of (Benirschke and Clifford), 924 (Abst.) infants, staphylococcic infections (Montgomery et al.), 1227
with ligated and nonligated umbilical cords, hemoglobin and hematocrit studies in (Bernstine and Ludmir), 66
prothrombin and proconvertin levels in vitamin K-blood-clotting studies during pregnancy and (Fresh, Adams, and Morgan). 927 (Abst.) retinal hemorrhage in (Duesberg and Tiburtins), 1366 (Abst.)
unexplained jaundice in, relationship of vitamin K to (Biskind and Herman), 1157 (Abst.)
Node resection, inguinal, femoral, and iliac, bilateral, radical vulvectomy with (Ulfelder), 1074

bilateral, radical vulvectomy (Ulfelder), 1074

(Ulfelder), 1074

Noninvolution of placental site (Paalman and McElin), 898

Nuclear sex chromatin pattern in dystrophia myotonica (Marshall and Thomas), 684 (Abst.)

and genital malformation with renal agenesis (Carpentier and Potter), 235

235

Nulliparous woman, lactation after hysterec-tomy in (Sachs), 204

Nurses, handbook of obstetrics and gynecology for (Clyne), 1152 (B. rev.)

Nursing, gynecologic, gynecology and (Miller and Avery), 1151 (B. rev.)

Nystatin, effect on neonatal candidiasis (thrush) (Harris et al.), 679 (Abst.)

Obesity, problem (Taller), 1144
Obstetric(al) anesthesia, terminal, by lumbar sympathetic paravertebral block (Riekse), 411
and synecological history, 1341
milestones—essays in eponymy (Speert),
455 (B. rev.)

hemorrhages, pregnancy toxemia and, patho-mechanism (Bieniarz), 385 patient, shock not related to blood loss, with Escherichia coli septicemia in (Ox-

orn), 567
point of view, "pre-diabetic" period from (Hagbard), 219 (Abst.) (Beck and Rosenthal), 457 (B. practice practical (Donald), problems.

rev.)
Obstetrics and gynecology, new name for?
(Speert), 212 (Pertinent com-

for nurses, rev.) handbook (Clyne), 1152 (B. postspinal headache in (Sweeney et al.),

textbook (Martins and Hartl), 1149 (B.

Occipitoposterior positions (King), 458 (B.

Operation, rev.)
Operation, radical vaginal, for carcinoma of cervix (McCall), 712
Ophthalmia neonatorum without prophylaxis, incidence (Solomons et al.), 513
Ovarian agenesis, factors in treatment (Sosnowski), 792
cycle and uterine motility (Corey, McGaughey, and Thornton), 20
cyst, neurilemmoma within right broad ligament mimicking (Gruhn, Hughes, and Aldisert), 1334
cystomas (De Santo, Bullock, and Moore), 1154 (Abst.)
cysts, neoplastic, movement of tritium-

cysts, neoplastic, movement of tritium-labeled water in (Peckham and Kiekhofer), 1120
follicle, movement of tritium-labeled water in (Peckham and Kiekhofer), 1012
hilus cells (Merrill), 1258
histology and physiology, 1258-1274
tumor, precocious puberty, and adrenal hyperfunction (Scarpa et al.), 821
tumors, 812-832

Ovaries.

rs, 812-832
varicocele, thrombosis, in postpartum
period (Meyer), 109
malformation, neoplasia with
(Stange), 1365 (Abst.)
cystic (Stein-Leventhal syndrome), reaction to gonadotropic hormones
(Stange and Schaumkell), 225
(Abst.)

(Stange and Schaumkell), 225
(Abst.)

Ovary, accessory and supernumerary (Wharton), 1101

benign cystic teratoma of, adenocarcinoma
of thyroid origin in (Mayberger),
817

chloroma (Hinkamp and Szanto), 812
dysgerminoma, associated with teratoma
(Jones), 825

right, arrhenoblastoma of (Johnston, Kernodle, and Saunders), 800

supernumerary and accessory (Wharton),
1101

1101

Ovulation, experimental induction, in Macaque monkey (Simpson and van Wage-nen), 223 (Abst.) Oxygen consumption decrease associated with prolonged administration of aceta-zolamide (Diamox) (Tenney and Tschetter), 921 (Abst.)

Oxygen-Cont'd

dissociation curves of nonpregnant, pregnant, and fetal blood, comparative
study (Prystowsky, Hellegers, and
Bruns), 489
prophylactic, effect on oxygen pressure
gradient between maternal and
fetal bloods (Prystowsky), 483
Oxytocic drugs, effects on blood flow to postpartium uterus (Assail Descripto

partum uterus (Assali, Dasgupta, and Kolin), 313 synthetic, clinical observations with toko-dynamometer (Middleton and

dynamometer (Middleton and Perry), 42
Oxytocin and renal cortical necrosis (Byrom and Pratt), 1363 (Abst.)
synthetic, clinical study of efficacy (Hollenback), 1158 (Abst.)
compatibility with anesthesia (Feldman, Forgaard, and Morris), 461 (Abst.)
Oxytocinase, blood, changes, during parturition (Hilton and Johnson), 479

Paz, autoradiography of carcinoma of uterus with (Stanicek), 225 (Abst.)
Pain relief in labor, anileridine for (Wizenberg et al.), 405
Pancreatitis, hyperlipemia and, hypercholesteremia and coronary artery discase complicating pregnancy (Adlersberg et al.), 851
Panhysterectomy, vaginal fluid subsequent to (Perl, Milles, and Shimozato), 285
Paravertebral lumbar sympathetic block in labor (LaSalvia, Copit, and Kondon), 1212
as terminal obstetrical anesthesia

don), 1212
as terminal obstetrical anesthesia
(Riekse), 411
Parturition, changes in blood oxytocinase during (Hilton and Johnson), 479
human, normal and abnormal labor (Miller,
Evans, and Haas), 455 (B. rev.)
Past, legacy of (Antony), 1341
Patho-mechanisms of late pregnancy toxemia
and obstetrical hemorrhages (Bieniarz), 385

eniarz), 385

Pelvic inflammatory disease, chronic, prednisone therapy in (Staemmler), 1367

sone therapy in (Staemmier), 1367
(Abst.)
superior mesenteric syndrome after
(Haddad and Decker), 1301
lymphadenec:omy, lymphocyst formation
after (Nelson and Huston), 1298
Pelvis, Robert (Kaiser), 1208
Perinatal mortality and morbidity, public
health aspects (Wallace), 522
in North Carolina' Memorial Hospital
(Flowers Weinel and Kirkland).

health aspects (Wallace), 522
in North Carolina' Memorial Hospital
(Flowers, Weinel, and Kirkland),
1157 (Abst.)
in primigravida over 30 years of age
(Lock et al.), 755
Perineal retractor, new (Pagano and Bobrow), 134,
Peripheral nervous system tumors of gynecologic interest (Gruhn, Hughes, and Aldisert), 1334
Peritonitis, meconium, with ascites resulting in dystocia (Wall), 1247
Personality, child, longitudinal studies (Stone and Onque), 1150 (B. rev.)
Pertinent comments, 212, 908
Pessary complications in management of uterine prolapse (McElin and Paalman), 643
Pharmacological action and placental transmission of barbiturates and thiobarbiturates (Flowers), 730
Pheochromocytoma diagnosed at cesarean section for labor obstructed by neurofibroma (Shell and Newton), 434
Phonocardiography and electrocardiography, fetal, present place in obstetrics for (Smyth and Farrow), 921 (Abst.)
Physiologic position for delivery (Howard), 1141 (Re-evaluation)

Physiology of pregnancy, 1-12, 303-321, 465-482, 844-867 reproductive (Nalbandov), 1152 (B. rev.) and therapy in labor, 13-46 vaginal, 279-289 Physiotherapy in obstetrics and gynecology (Heardman and Ebner), 917 (B. rev.)

Pituitary FSH, human, clinical effect (Gemzell, Diczfalusy, and Tillinger), 682 (Abst.)

lacenta accreta, spontaneous rupture of gravid uterus due to (Golden and Betson), 890 circulation (Arts), 918 (B. rev.) morphologic and functional aspects (Snoeck), 459 (B. rev.) previa, hemorrhage in (Kimbrough), 1165 rupture of marginal sinus, and abruptio placentae (Ferguson and Halton), 947 947

lacental circulation, arteriographic study (Borell, Fernstrom, and Westman), 922 (Abst.) site, noninvolution (Paalman and McElin),

898

and venous drainage of pregnant uterus (Bieniarz), 385 ansmission of barbiturates and thiobar-biturates and pharmacological ac-tion on mother and infant (Flowtransmission tion on ers). 73 730

Pneumomediastinum and aspiration pneumonia complicating labor (Elsinger and Berk), 438

Berk), 438
Pneumonia, aspiration, pneumomedias and, complicating labor (Ei and Berk), 438
Poisoning, transplacental naphthalene ziulewicz, Dick, and Chia pneumomediastinum (Eisinger

Chiarulli). 519

ovaries (Stein-Leventhal syndrome), reaction to gonadotropic hormones (Stange and Schaumkell), 225 (Abst.), international dilemma (Osborn), Polycystic

Population, international difference of the state of delivery on, colposcopic study (Zimskind and Lang), 223

Position, physiologic, for delivery (Howard), 1141 (Re-evaluation)
Postmaturity, death from, and life from induction of labor, choice (Theobald), 686 (Abst.)
Postmenopausal uterine bleeding (Te Linde and Reis), 1347 (Clinical problems)

lems)

breast manifestations, hormone therapy to control (Gold et al.), Postpartum

thrombosis

sis of ovarian vein varicocele (Meyer), 109 effects of oxytocic, vasopressor, and vasodepressor drugs on blood flow to (Assali, Dasgupta, and Kolin), 313 uterus.

flow to (Assaii, Dasgapta, and Kolin), 313 Postspinal headache in obstetrics (Sweeney et al.), 415 Postural effects on cardiovascular status in pregnancy (Quilligan and Tyler),

Potassium, sodium and, total exchangeable, in nonpregnant women and nor-mal and pre-eclamptic pregnancy (MacGillivray and Buchanan), 1361 (Abst.)

Precocious puberty and adrenal hyperfunc-tion due to ovarian tumor (Scarpa et al.), 821 "Pre-diabetic" period from obstetric point of view (Hagbard), 219 (Abst.)

Prednisone therapy in chronic pelvic inflam-matory disease (Staemmler), 1316 (Abst.)

Pre-eclampsia, osia, action of Serpasil on (Hopf-gartner), 224 (Abst.) Pre-eclampsia-Cont'd

Pre-eclampsia—Cont'd
fulminating, with cesarean section under
hypnosis (Winkelstein and Levinson), 420
influence of chlorothiazide on water and
electrolyte excretion in (de Alvarez
and O'Lane), 681 (Abst.)
liver in (Antia et al.), 1358 (Abst.)
recurrent hydatidiform mole complicated by
(Marcus and Quattlebaum), 881
Pre-eclamptic pregnancy, total exchangeable
sodium and potassium in nonpregnant women and in normal and
(MacGillivray and Buchanan), 1361
(Abst.) (Abst.)

es, normal, in juvenile hypothyroid patient (Paz-Carranza, Perlmutter, and Prigerson), 1199 Pregnancies.

Pregnancy, abdominal, endocrine studies in two cases (Siegler et al.), 369 achieved by autoinsemination (Walters and Kaufman), 274 acute appendicitis in (Burwell and Brooks),

adrenal cortical function during (Jailer et al.), 1 na of

al.), 1
carcinoma of breast and (Randall and Schmitz), 1353 (Clinical problems)
cardiovascular status in, postural effects on (Quilligan and Tyler), 465
cervical (Ashitaka et al.), 351
mucus studies in, importance (Schwalenberg and Efstation), 860
complicated by Addison's disease (Sluder), 808

808

by previous bilateral total adrenalectomy (Estrada et al.), 1176
complications, 546-581, 890-907, 1172-1201
deaths from Asian influenza associated with (Freeman and Barno), 1172
defibrination syndrome in (Sharp et al.), 685 (Abst.)
diabetes insipidus and (Giardini and Colque),

diabetes insipidus and (Giardini and Colque), 220 (Abst.)
early, intracranial venous thrombosis in (Stevens and Ammerman), 104
ectopic, 340-374
advanced (Clark and Bourke), 340
effect on hepatolenticular degeneration (Wilson's disease) (Bihl), 1182
embolism and thrombosis in, 96-111
endotoxin shock and generalized Shwartzman reaction in (McKay, Jewett, and Reid), 546
giant hydronephrosis complicating (Bernstine, LeBlanc, and Richardson), 431
glandular structures of cervix uteri during (Fluhmann), 990
heart disease complicating, conservative

disease complicating, conservative management (Smith and Gatenby), 679 (Abst.) heart hemangioma of cervix complicating (Lovett),

424

hyperlipemia and pancreatitis, hypercholes-teremia and coronary artery disease complicating (Adlersberg et al.), 859 and labor, complications, 424-444

and labor, complications, 424-444
effects on respiratory pattern of newborn
infant (Calkins and Miller), 1005
leukemia, acute granulocytic in (Rothberg,
Conrad, and Cowley), 921 (Abst.)
liver in (Antia et al.), 1358 (Abst.)
malformations of uterus and, 1202-1211
megaloblastic anemia of (Giles and Shuttleworth), 684 (Abst.)
in noncommunicating rudimentary horn
(Gergely and Mason), 1202
nontoxemic hypertension in, symposium
(Morris and Brown), 458 (B. rev.)
normal and abnormal, effect of prophylactic
oxygen on oxygen pressure gradient
between maternal and fetal bloods
in (Prystowsky), 483
immunologic characteristic of serum of
(MacLaren et al.), 939

Pregnancy, normal-Cont'd

and pre-eclamptic, total exchangeable sodium and potassium in nonpregnant
women and (MacGillivray and Buchanan), 1361 (Abst.)
and toxemic, renal handling of sodium
and water in (de Alvarez, Bratvold,
and Harding), 375
occult blood in stoois in, incidence (Dickens
and Planas), 864
physiology, 1-12, 303-321, 465-482, 844-867
postural effects on cardiovascular status in
(Quilligan and Tyler), 465
prevention, by Graefenberg ring method
(Oppenheimer), 446 (Re-evaluation)
prolonged (Lindgren, Normann, and Viberg),
219 (Abst.)
renal failure, acute, in (Knapp and Hellman), 570
function in, in normal women (Sims and
Krantz), 923 (Abst.)
rubella during (Blattner), 925 (Abst.)
in (Pearse), 228 (Correspondence)
ruptured cerebral aneurysm in (Wacker),
1189
serum lactic dehydrogenase in (Linton and and pre-eclamptic, total exchangeable sodi-

ruptured cerebral aneurysm in (Wacker), 1189
serum lactic dehydrogenase in (Linton and Miller), 11
and spontaneous delivery after operation for congenital atresia of vagina (Pilkington), 804
surgical complications, 112
suture of incompetent cervix during maternal death following (Dunn, Robinson, and Steer), 335
term, metallic intrauterine foreign body in (Arms'rong and Andreson), 442
test by electroplating of urine (Hartung and DeVauent), 1250
thrombocytopenia in, following splenectomy (Rogers), 806
toxemia (see Toxemia of pregnancy)
toxemic, renal handling of sodium and water in (de Alvarez, Bratvold, and Harding), 375
trophoblast in circulating blood during (Douglas et al.), 960
tubal, following homolateral salpingectomy (Fulsher), 355
twin, repair of incompetent cervix in case of (Frank and Rubovits), 333
unwanted, willful exposure to (Lehfeldt), 661
urinary tract infection, acute, in (Mulla),

urinary tract infection, acute, in (Mulla), 578

volvulus associated with (Malkasian, Welch, and Hallenbeck). 112 vomiting of (Coppen), 687 (Abst.)

weight gain and toxemia, relationship (Fish et al.), 743
regnanediol and 17-hydroxycorticosteroid excretion during labor and post partum, parallel investigation (Cekon and Ehrlich), 1159 (Abst.) Pregnanediol

Pregnant and fetal blood, oxygen dissociation curves, comparative study (Prystowsky, Hellegers, and Bruns), 489 rudimentary horn of bicornuate uterus, rupture (Goldman and Eckerling), 1205

Q

ture (Goldman and Eckerling), 1205 contractility, inhibitory action of Halothane on (Embrey, Garrett, and Pryer), 1326 (Abst.) s drainage, placental site and (Bieniarz), 385 rate of hydrocortisone clearance from plasma in (Christy et al.), 683 (Abst.)

toxemic, total body water, sodium space, and total exchangeable sodium in (Plentl and Gray), 472 toxeplasmosis suspect, sulfonamide prophylaxis in (Welsse), 1365 (Abst.)

Prematurity and spontaneous abortion (Gray, Tupper, and Rowse), 325

Presentation, errors (Flelds and Nelson), 539 and prolapse of umbilical cord (Norburn), 1234

Primigravida over 30 years of age perinetal

Primigravida over 30 years of age, perinatal mortality in (Lock et al.), 755

Procidentia, uterine, with incarceration (Brody), 647
Proconvertin and prothrombin levels in new-

Procidentia, uterine, with incarceration (Brody), 647
Proconvertin and prothrombin levels in newborn, vitamin K-blood-clotting studies in pregnancy and (Fresh, Adams, and Morgan), 927 (Abst.)
Progesterone levels, estrogen and, in fetal and maternal plasma at parturition (Aitken et al.), 1362 (Abst.)
Progestin-induced pseudopregnancy, effects on endometriosis (Andrews, Andrews, and Strauss), 776
Prolapse, genital, repair (Gibson), 1275 of umbilical cord, presentation and (Norburn), 1234 uterine, pessary complications in management (McElin and Paalman), 647
Prolapsed cord, death from, and life from induction of labor, choice (Theobald), 686 (Abst.)
Promazine, intravenous, gangrene after (Shell, McIntyre, and Castellano), 1219
Proteinuria of renal tubular disorders (Butler and Flynn), 1359 (Abst.)
In toxemia of pregnancy, causes (Friedberg), 1367 (Abst.)
Prothrombin and proconvertin levels in newborn, vitamin K-blood-clotting levels in pregnancy and (Fresh, Adams, and Morgan), 927 (Abst.)
Pseudoherinaphroditism, female, nonspecific, genital malformation with (Carpentier and Potter), 235
Pseudopregnancy, progestin-induced, effects on endometriosis (Andrews, Andrews, and Strauss), 776
Puberty, precocious, and adrenal hyperfunction due to ovarian tumor (Scarpa et al.), 821
Public health aspects of perinatal mortality and problidity (Wellege), 522

et al.), 821

Public health aspects of perinatal mortality and morbidity (Wallace), 522

Puerperal breast engorgement, prevention with large doses of long-acting estrogen (King), 80

inversion, managed by Haultain technique (Easterday and Reid), uterus, 1224

n, corpus luteum hormone and 17-ketosteroid excretion during labor and (Cekon and Ehrlich), 464 Puerperium, (Abst.)

hemoglobin changes in labor and (Miller, Williams, and Macarthur), 303 renal function in, in normal women (Sims and Krantz), 923 (Abst.) ruptured cerebral aneurysm in (Wacker), 1189

Puff, auctioneer's (King), 214 (Pertinent com-ments)

R

Radiation, cellular changes in vaginal and buccal smears after: index of ra-diocurability of cervix carcinoma (Jones et al.), 1083 Radical vaginal operation for cervix carcinoma

Radical vaginal operation for cervix carcinoma (McCall), 712
Radiocurability of cervix carcinoma, index (Jones et al.), 1083
Radiography, gynecologic, including breast (Dalsace a n d Garcia-Calderon), 456 (B. rev.)
Radiophosphorus, autoradiography of carcinoma of uterus with (Stanicek), 225 (Abst.)
Rectovaginal septum, adenocarcinoma of probably arising from endometrio-

nal septum, adenocarcinoma of, probably arising from endometriosis (Lash and Rubenstone), 299 tion, 445, 1141 effect on electively induced labor (Babcock and Peterson), 33 accelerating first stage of labor (Rothman, Bentley, and Floyd), 38 Re-evaluation, Relaxin, effect

Renal agenesis, nuclear sex and genital mal-formation in 48 cases (Carpentier and Potter), 235

Renal-Cont'd

necrosis, oxytocin and (Byrom and Pratt), 1363 (Abst.) acute, in pregnancy (Knapp and Hellman), 570 in pregnancy and puerperium in normal women (Sims and Krantz), cortical

function

normal women (Sims and Krantz),
923 (Abst.)
handling of sodium and water in normal
and toxemic pregnancy (de Alvarez,
Bratvold, and Harding), 375
maturity of infants of toxemic mothers
(Beaudry and Landing), 494
shutdown, acute, toxemia, abruptio placentae, hypofibrinogenemia, and paralytic ileus complicating case of
prepregnancy hypertension (Clark
and Bennett), 1169
tubular disorders, proteinuria of (Butler
and Flynn), 1359 (Abst.)
teproductive physiology (Nalbandov), 1152

ve physiology (B. rev) Reproductive (Nalbandov),

(B. rev.)
Respiratory pattern of newborn infant, effects of pregnancy and labor on (Calkins and Miller), 1005
Retention, urinary, postoperative and postpartum, treatment with dihydroer g o t a m i n e (Wertsch), 1158 (Abst.)

Retinal hemorrhage in newborn (Duesberg and Tiburtius), 1366 (Abst.)
Retractor, perineal, new (Pagano and Bobrow), 134
Retrograde ejaculation of semen, sterility due to (Walters and Kaufman), 274
Rheumatoid arthritis, serum seromucoid, hexose, and hexosamine in (Gray), 322

Ring, Graefenberg, prevention of pregnancy by (Oppenheimer), 446 (Re-evalua-

by (Opperation)
tion)
Robert pelvis (Kaiser), 1208
Rooming-in and nursery care, comparison of staphylococcic infections encountered with (Montgomery et al.),

Roster of American obstetrical and gyne-

cological societies, 230 internal, mechanism, and application to malrotation (D'Esopo), 530 luring pregnancy (Blattner), 925 during Rubella

(Abst.) nancy (Pearse), 228 (Correspond-

in pregnancy (Pearse ence) of marginal of marginal sinus of placenta, abruptio placentae and (Ferguson and Hatton), 947 spontaneous, of gravid uterus due to placen-ta accreta (Golden and Betson), Rupture

Salpingectomy, homolateral, tubal pregnancy following (Fulsher), 355 Sarcoma borryoides (Crawford), 618

following (Fulsher), 355
Sarcoma botryoides (Crawford), 618
(Hill, Lebherz, and McMahon), 621
mixed mesodermal, of corpus uteri associated with bilateral thecoma (Laurain and Monroe), 613
of uterus, 604-627
(Radman and Korman), 604
Schistosoma mansoni, gastric hemorrhage due to, maternal death from (Kahane and Martin), 1194
Screening, mass, for uterine cancer, dual smear examinations in (Song, Fanger, and Murphy), 1309
Semen, retrograde ejaculation, sterility due to (Walters and Kaufman), 274
Septicemia, Escherichia coli, shock not related to blood loss with, in obstetric patient (Oxorn), 567
Seromucoid, serum, in spontaneous abortion and rheumatoid arthritis (Gray), 322
Serotonin and menopausal flush (Munsick),

Serotonin and menopausal flush (Munsick), 147

Serpasil, action in pre-eclampsia (Hopfgart-ner), 224 (Abst.) Serum lactic dehydrogenase in pregnancy

Serum lactic dehydrogenase in pregnancy (Linton and Miller), 11
of normal pregnancy, immunologic characteristic of (MacLaren et al.), 939
Sex and adolescent (Davis), 456 (B. rev.) chromatin, nuclear, pattern in dystrophia myotonica (Marshall and Thomas), 684 (Abst.)
nuclear, and genital malformation with renal agenesis (Carpentier and Potter), 235

agenesis (Carpentier and Potter),
235

Sexual tones in marriage of sterile and oncei sterile female (Rommer and Rommer), 221 (Abst.)

Sexuality, female, changes, after adrenalectomy (Waxenberg, Drellich, and
Sutherland), 683 (Abst.)

Shock due to infection, adrenal cortical function and cortisol metabolism in
(Melby and Spink), 924 (Abst.)

not related to blood loss, with Escherichia
coli septicemia in obstetric patient (Oxorn), 567

Shwartzman reaction, generalized, in pregnancy, endotoxin shock and (McKay,
Jew-2t\*, and Reid), 546

Smear examinations, dual, in mass screening
for uterine cancer (Song, Fanger,
and Murphy), 1309

Smears, cervical and nasal, comparative
study (Davis and Abou-Shabanah),
222 (Abst.)

vaginal and buccal, after radiation, cellular
changes: index of radiocurability
of cervix carcinoma (Jones et al.),
1083

Smegma in carcinoma of cervix (Smatko), 226

1083 Smegma in carcinoma of cervix (Smatko), 226 (Correspondence)

horse, carcinogenic action in mouse vagina, investigation (Sala), 1366 (Abst.)

investigation (Sala), 1366 (Abst.)

Smith, Albert Holmes, study in courage (Scheffey), 929

Sodium chloride, hypertonic, effect on contractility in myometrium (Hendricks and Tucker), 13

and potassium, total exchangeable, in nonpregnant women and normal and pre-eclamptic pregnancy (Mac-Gillivray and Buchanan), 1361 (Abst.) Abst.)

space and total exchangeable sodium, total body water and, in normal and toxemic pregnant women (Plentl and Gray), 472

and water, renal handling of, in normal and toxemic pregnancy (de Alvarez, Bratvold, and Harding), 375

South Atlantic Association of Obstetricians and Gynecologists, transactions of twenty-first annual meeting, 697

Specialty, our, new name for? (Speert), 212 (Pertinent comments) Sperm, homologous, injection, infertility in female guinea pigs induced by

sperm, nomologous, injection, intertrity in female guinea pigs induced by (Katsh), 276 motility, chemotaxis as factor in (Schwartz, Brooks, and Zinsser), 221 (Abst.)

Spermatozoa, transport into uterus of rabbit (Noyes, Adams, and Walton), 220 (Abst.)

(Abst.) Spinal cord, injuries to (Stern and

Spinal cord, birth injuries to (Stern and Rand), 498

Splenectomy, thrombocytopenia in pregnancy following (Rogers), 806

Squamocolumnar junction and endocervical glands, relationship to site of origin of carcinoma of cervix (Thornton, Fox, and Smith), 1060

Squamous-cell carcinoma of vulva in young women (Lash and Davis), 841

Staphylococcal infection in maternity hospital (Gillespie, Simpson, and Tozer), 1360 (Abst.)

Staphylococcic colonization of mothers and newborn infants (Montgomery et al.), 1227

Staphylococcus type 80 epidemic in maternity hospital (Timbury et al.), 1361 (Abst.)

(Abst.)
Stein-Leventhal syndrome (Stein), 925 (Abst.)
pathologic anatomy (Plate), 462 (Abst.)
polycystic ovaries, reaction, to gonadotropic hormone (Stange and
Schaumkell), 225 (Abst.)
Sterile female, sexual tones in marriage of
(Rommer and Rommer), 221
(Abst.)

Sterility.

(Rommer and Rommer), 221 (Abst.)
anovulatory, hypercorticalism as cause (Bagnati, Montes, and Zapata), 678 (Abst.)
retrograde ejaculation of semen (Walters and Kaufman), 274
World Congress on Fertility and, proceedings (Tesauro, editor), 1151 (B. rev.) due Second

Second Works proceedings (Tesauro, care)

(B. rev.)
Steroid formation by adrenal tissues from hypertensives (Cooper et al.), 923 (Abst.)
Stools, occult blood in, in pregnancy, incidence (Dickens and Planas), 864
Stress incontinence, anterior vaginal suspension operation in (Durfee), 628 urinary, cinefluorographic studies (Lund, Fullerton, and Tristan), 706
Sulfonamide prophylaxis in toxoplasmosis suspect pregnant women (Weisse),

Sulfonamide prophylaxis in toxoplasmosis suspect pregnant women (Weisse), 1365 (Abst.)

Superior mesenteric syndrome after pelvic inflammatory disease (Haddad and Decker), 1301

Supine and lateral postures, comparison of effects on cardiovascular status in pregnancy (Quilligan and Tyler), 465

Surgery in cervix corelarms, 101 100

Surgery in cervix carcinoma, 191-199
Graves' synopsis (Wakely), 918 (B. rev.)
gynecologic, vasopressin as hemostatic in
(Dillon), 1285
textbook (Moseley), 458 (B. rev.)
Surgical anatomy, Callander's (Anson and
Maddock), 456 (B. rev.)
complications of pregnancy, 112
management, total (Hardy), 919 (B. rev.)
procedures and complications, 1275-1303
Suspension, anterior vaginal, operation (Durfee), 628

Suspension, anterior vaginai, operation fee), 628
Sympathetic block, paravertebral lumbar, in labor (LaSalvia, Copit, and Kondon), 1212
Sympathetic, lumbar, paravertebral block as terminal obstetrical anesthesia (Riekse), 411

terminal obstetrical anesthesia (Riekse), 411
Syndrome, Meigs' (Justen), 830
Stein-Leventhal (Stein), 925 (Abst.)
pathologic anatomy (Plate), 462 (Abst.)
polycystic ovaries, reaction to gonadotropic hormone (Stange and Schaumkell), 225 (Abst.)
Synthetic oxytocin, clinical study of efficacy (Hollenback), 1158 (Abst.)
Syntocinon, compatibility with a nesthesia (Feldman, Forgaard, and Morris), 461 (Abst.)
Systemic disease, menstruation and (Rogers),

Systemic disease, men 926 (Abst.) menstruation and (Rogers),

T

Tables turn (Collins), 697
Teratoma, benign cystic, adenocarcinoma of thyroid origin in (Mayberger), 817 dysgerminoma of ovary associated with (Jones), 825
Testicular biopsy in male infertility (Zenisck and Herant), 1367 (Abst.)
Testosterone, effect on experimental endometriosis in rhesus monkeys (Scott and Wharton), 1020
Textbook of obstetrics (Martins and Hartl), 1149 (B. rev.)
Thecoma, bilateral, mixed mesodermal sarcoma of corpus uteri associated with

coma of corpus uteri associated with (Laurain and Monroe), 613

Thecoma with virilization (Nokes, Claiborne, and Reingold), 722
Thiobarbiturates; placental transmission, and pharmacologic action in mother and infant (Flowers), 730
Thrombocytopenia in pregnancy following splenectomy (Rogers), 806
Thrombosis, embolism and, in pregnancy, 96-11
intracranial, vanous, in carly, pregnancy

intracranial venous, in early pregnancy
(Stevens and Ammerman), 104
of ovarian vein varicocele in postpartum
period (Meyer), 109
Thrush (candidiasis), effect of nystatin on:
method of eradicating from hospital nurseries (Harris et al.), 679
(Abst.)
Thyroid function

(Abst.)
Thyroid function, maternal, effect on fetal thyroid function and development (Carr et al.), 632 (Abst.)
origin, adenocarcinoma of, in beniem cystic teratoma (Mayberger), 817
Tissue culture, endometrial cells in, behavior (Papanicolaou and Maddi), 156
fetal, autolyzed, cytomegalic inclusions in (Belter and Camilo), 1243
Tokodynamometer, clinical observations of synthetic oxytocic with (Middleton and Perry), 38
Toxemia, 375-404
pre-eclamptic, fulminating

pre-eclamptic, fulminating, with cesarean section under hypnosis (Winkel-stein and Levinson), 420 of pregnancy, etiology (Sophian), 688 (Cor-

respondence) ly) (Jeffcoate and Scott), (Correspondence) (reply)

(Correspondence)
hypertensive lineage and (Kaku and Nagata), 399
influence of chlorothiazide on water and electrolyte excretion in (de Alvarez and O'Lane), 681 (Abst.)
and o b stetrical hemorrhages, pathomechanism (Bieniarz), 385
proteinistic in causes (Friedberg), 1367

in, causes (Friedberg).

mechanism (Bieniarz), 385
proteinuria in, causes (Friedberg), 1367
(Abst.)
superimposed, abruptio placentae, hypofibrinogenemia, acute renal shutdown, and paralytic ileus complicating case of prepregnancy hypertension (Clark and Bennett), 1169
and weight gain in pregnancy, relationship (Fish et al.), 743
Toxemic mothers, renal maturity of infants of (Beaudry and Landing), 494
pregnancy, renal handling of sodium and water in (de Alvarez, Bratvold, and Harding), 375
pregnant women, total body water, sodium space, and total exchangeable sodium in (Plenti and Gray), 472
Toxoplasmosis suspect pregnant women, sulfonamide prophylaxis (Weisse), 1365 (Abst.)
Trachelotome, new, for cervical biopsy (Averbergh)

Trachelotome, new, for cervical biopsy (Averbach), 1312

Transactions of the American Gynecological Society, eighty-second annual meeting, 929

of South Atlantic Association of Obstetricians and Gynecologists, twenty-first annual meeting, 697
ranscortin, corticosteroid-binding protein of plasma (Slaunwhite and Sandberg),

Transcortin.

Transcortin, corticosteroid-binding protein of plasma (Slaunwhite and Sandberg), 684 (Abst.)

Transplacental naphthalene poisoning (Anziulewicz, Dick, and Chiarulli), 519

Trichomonal infection, aid for treating (Rogers), 226 (Correspondence) vaginals and Candida, routine culture examinations for (Clark and Solomon) 1214

aminations for (Clark and Solo-mons), 1314

Tritium-labeled water, movement in human ovarian follicle (Peckham and Kiekhofer), 1012
in neoplastic cystic structures (Peckham and Kiekhofer), 1120

Trophoblast in circulating blood during preg-nancy (Douglas et al.), 960

Trophoblastic tumors of testis, metastatic, therapy with Methotrexate (Bruckner), 921 (Abst.)

Tubal pregnancy following homolateral salpingectomy (Fulsher), 355

Tube and cervix, epithelium, in patients with endometrial carcinoma (Chun, Gong, and Roddick), 174

Tumor, ovarian, precocious puberty, and adrenal hyperfunction (Scarpa et al.), 821

umors, chorionic, 868-889 metastatic, trophoblastic, of testis, therapy with Methotrexate (Bruckner), 921 (Abst.) Tumors.

(Abst.)
ovarian, 812-832
of peripheral nervous system of gynecologic
interest (Gruhn, Hughes, and
Aldisert), 1334
vulval and vaginal, 290-302
Turning the tables (Collins), 697
Twin, ectopia cordis in (Hurwitt and Lebendiger), 1155 (Abst.)
pregnancy, repair of incompetent cervix in
case of (Frank and Rubovits), 333

Umbilical cord, prolapse, presentation and (Norburn), 1234
simplified ligation with new instrument and technique (Baden, Gran, and Bennack), 136
cords, ligated and nonligated, bacteriologic studies in (Bernstine, Ludmir, and Fritz), 69

69 hemoglobin and hematocrit studies in newborn with (Bernstine and Lud-mir), 66

Urea, equilibration between mother and fetus

Urea, equilibration between mother and fetus (McGaughey et al.), 844
Urethra, carcinoma of, primary treatment in Department of Gynecology at University of Wirzburg in last 30 years (Knopp), 1158 (Abst.)
cinefluorographic studies of bladder and (Lund, Fullerton, and Tristan), 706
Urinary estrogens in women (Smith, Smith, and Gavian), 1028
retention, postoperative and postpartum, treatment with dihydroergotamine (Wertsch), 1158 (Abst.)
tract infection, acute, in pregnancy (Mulla), 578

578

Urine, electroplating test of, for prexmancy (Hartung and DeVauent), 1250
Usage, common, of English language (Barnes), 915 (Pertinent comments)
Uterine artery and vein, arteriovenous aneurysm, following total abdominal hysterectomy (Wideman, Gravlee, and Jones), 200
bleeding, dysfunctional (Israel and Peckham), 672 (Clinical problems)
postmenopausal (Te Linde and Reis), 1347 (Clinical problems)
blood flow and metabolism, measurement (Assali, Dasgupta, and Kolin), 313 cancer, dual smear examinations in mass screening for (Song, Fanger, and Murphy), 1309
muscle, spontaneous motility, in vitro (Corey, McGaughey, and Thornton), 200

procidentia with incarceration (Brody), procidentia with incarceration (Brody), 647
prolapse, peasary complications in management (McElin and Paalman), 643
tube and cervix, epithelium, in patients with
endometrial carcinoma (Chun, Gong,
and Roddick), 174
Uteroabdominal menstrual fistula (Kirkland),

Uteroplacental circulation (Arts), 918 Uterotubal insufflation, effects of light on (Polishuk), 223 (Abst.)

Uterus adenocarcinoma, effects of preoperative irradiation on (Schmitz, Smith, and Fetherston), 1048
bicornis unicollis, pregnancy in noncommunicating horn of (Gergely and Mason), 1202
bicornuate, rupture of pregnant rudimentary horn of (Goldman and Eckerling), 1205
carcinoma (see Carcinoma of uterus)

carcinoma (see Carcinoma of uterus)
gravid, spontaneous rupture, due to placenta
accreta (Golden and Betson), 890
malformations and pregnancy, 1202-1211
postpartum, effects of oxytocic, vasopressor,
and vasodepressor drugs on blood
flow to (Assali, Dasgupta, and
Kolin), 313

Kolin), 313
pregnant, contractility, inhibitory action of
Halothane on (Embrey, Garrett,
and Pryer), 1362 (Abst.)
venous drainage, placental site and
(Bieniarz), 385
puerperal, inversion, managed by Haultain
technique (Easterday and Reid),

1224

of rabbit, transport of spermatozoa into (Noyes, Adams, and Walton), 220 (Abst.)

604-627 sarcoma, (Radman and Korman), 604

#### V

Vagina, congenital atresia, pregnancy and spontaneous delivery after operation for (Pilkington), 804 melanoma, primary malignant, of (Freund, Kegel, and Dugger), 290 Vaginal acids, study of (Hunter and Nicholas), 282

radiation: index of radiocurability of cervix carcinoma (Jones et al.), and buccal

1083

candidiasis, new agent for treatment (Lapan), 1320
fluid, quantity (Stone and Gamble), 279
subsequent to panhysterectomy (Perl, Milles, and Shimozato), 285
hysterectomy, radical, extraperitoneal lymphadenectomy and, for cervix cancer (Mitra), 191
operation, radical, in cervix carcinoma (McCall), 712
physiology, 279-289
relaxation, descensus and, 628-649
suspension operation, anterior (Durfee), 628
and yulval tumors, 290-302

and vulval tumors, 290-302 Vaginitis, 1314-1323 emphysematosa (Hoffman and Grundfest),

Trichomonas, aid for treati 226 (Correspondence) treating (Rogers).

226 (Correspondence)
Varicocele, ovarian vein, thrombosis, in postpartum period (Meyer), 109
Vasodepressor drugs, effect on blood flow to
postpartum uterus (Assali, Dasgupta, and Kolin), 313
Vasopressin as hemostatic in gynecologic
surgery (Dillon), 1285
Vasopressor drugs, effect on blood flow to
postpartum uterus (Assali, Dasgupta, and Kolin), 313
Vein, ovarian, varicocele, thrombosis, in post-

gupta, and Kolini, 515

Vein, ovarian, varicocele, thrombosis, in postpartum period (Meyer), 109

Venezuelan Congress on Obstetrics and Gynecology, 1160 (Item)

Venous drainage of pregnant uterus, placental
site and (Bieniarz), 385

Venous thrombosis, intracranial, in early
pregnancy (Stevens and Ammerthrombosis, pregnancy (Stevens and Ammer-

man), 104
Vesicovaginal fistula (Schneiderman at Stream), 1155 (Abst.)
fistulas, follow-up (Wenig), 1158 (Abst.)

- Virilization, thecoma with (Nokes, Claiborne, and Reingold), 722

  Vitamin K, relationship to unexplained jaundice in newborn (Biskind and Herman), 1157 (Abst.)

  K-blood-clotting studies during pregnancy and prothrombin and proconvertin levels in the newborn (Fresh, Adams, and Morgan), 927 (Abst.)

  Volvulus associated with pregnancy (Malkasian, Welch, and Hallenbeck), 112

- kasian, Welch, and Hallenbeck).
  112
  Vomiting of early pregnancy (Coppen), 687
  (Abst.)
  Vulva, carcinoma (see Carcinoma of vulva)
  diseases (Calandra and Sammarino), 1150
  (B. rev.)
  hemangiopericytoma of (de Sousa and
  Lash), 295
  Vulval and vaginal tumors, 290-302
  Vulvectomy, radical, with bilateral inguinal,
  femoral, and illac node resection
  (Ulfelder), 1074

nd electrolyte excretion in pre-eclampsia, influence of chlorothia-zide on (de Alvarez and O'Lane), 681 (Abst.) Water and

- Water-Cont'd
- Water—Cont'd
  sodium and, renal handling of, in normal
  and toxemic pregnancy (de Alvarez, Bratvold, and Harding), 375
  total body, sodium space, and total exchangeable sodium in normal and
  toxemic pregnant women (Plenti
  and Gray), 472
  tritium-labeled, movement in human ovarian follicle (Peckham and Kiekhofer), 1012
  in neoplastic cystic structures (Peckham and Kiekhofer), 1120
  Weight gain in pregnancy and toxemia, relationship (Fish et al.), 743
  Wilson's disease, effect of pregnancy on
  (Bihl), 1182
  Women, diseases (Roques, Beattie, and
  Wrigiey), 1152 (B. rev.)
  World Congress on Fertility and Sterility,
  second, proceedings (Tesauro, editor), 1151 (B. rev.)

Young women, ca (Garcia cancer of endometrium in ia and Constantino), 1155 (Abst.)

DOES NOT CIRCULATE

DECEMBER, 1959 VOL. 78, NO. 6

American Journal of OBS

DEC 11 1959 /

# OBSTETRICS AND GYNECOLOGY

INDEX NUMBER

Editor in Chief
HOWARD C. TAYLOR, IR.

Editors

JOHN I. BREWER

ALLAN C. BARNES

#### Official Publication

AMERICAN GYNECOLOGICAL SOCIETY

AMERICAN ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS
CENTRAL ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS
SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA
SOUTH ATLANTIC ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS

The Journal is also the Official Publication of the Societies listed on page 6.



decisive therapy in a delicate matter



Vaginal Gream

wide-spectrum microbicide
antitrichomonal • antibacterial • antimonilial

provides potent microbicidal action in vaginal infections, including trichomoniasis, moniliasis and nonspecific vaginitis

Effective—Cured or markedly improved—within 2-3 weeks—86 per cent of 250 patients with various types of vaginal infections.<sup>1,2</sup>

Broad spectrum—Pathogens included Trichomonas vaginalis, Candida albicans and Hemophilus vaginalis, as well as other gram-negative and gram-positive organisms.<sup>1,2</sup>

**Safe**—Closed-patch skin tests proved Triburon Chloride, the active ingredient of Triburon Vaginal Cream, "... to be nonirritating... not sensitizing...."<sup>3</sup>

Nonstaining, odorless Triburon Vaginal Cream is also suited for use during pregnancy, menstruation, for senile vaginitis with conjunctive therapy, for preoperative, postoperative and postpartum prophylaxis, after cauterization, conization, irradiation.

Composition: Triburon Vaginal Cream contains 0.1% concentration of Triburon in a white, hydrophilic cream base.

Dosage: One applicatorful of Triburon Vaginal Cream should be introduced into the vagina every night for 2 weeks. If necessary, the course of therapy may be repeated.

Caution: Triburon is virtually nonsensitizing and nonirritating but if evidence of sensitization occurs, use of the cream should be discontinued.

Supplied: 3-ounce tubes with 18 disposable applicators.

References: 1. J. J. McDonough and N. Mulla, to be published. 2. Reports on file, Roche Laboratories. 3. R. C. V. Robinson and L. E. Harmon, Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.

ROCHE LABORATORIES



Division of Hoffmann-La Roche Inc . Nutley 10 . N. J.

#### CONTENTS

ous

lus

on, ro-

use

v.

J.



#### for December, 1959

#### OBSTETRICS

Antepartum Hemorrhage	
ANTEPARTUM HEMORRHAGE	
Robert A. Kimbrough, M.D., Philadelphia, Pa	1161
SUPERIMPOSED TOXEMIA, ABRUPTIO PLACENTAE, HYPOFIBRINOGENEMIA, ACUTE RENAL SHUTDOWN, AND PARALYTIC ILEUS COMPLICATING A CASE OF PREPREGNANCY HYPERTENSION	
John F. J. Clark, M.D., and Ridgely Bennett, M.D., Washington, D. C	1169
Complications of Pregnancy	
DEATHS FROM ASIAN INFLUENZA ASSOCIATED WITH PREGNANCY	
D. W. Freeman, M.D., and A. Barno, M.D., Minneapolis, Minn	1172
PREGNANCY COMPLICATED BY PREVIOUS BILATERAL TOTAL ADRENALECTOMY	
William J. Estrada, M.D., R. Z. Hundley, M.D., J. E. Norris, M.D., and T. G. Gready, M.D., Houston, Texas	1176
THE EFFECT OF PREGNANCY ON HEPATOLENTICULAR DEGENERATION (WIL-	
SON'S DISEASE)  John H. Bihl, M.D., Northville, Mich	1182
RUPTURED CEREBRAL ANEURYSM IN PREGNANCY AND PUERPERIUM	1100
Maxwell N. Wacker, M.D., Chicago, Ill	1189
Schistosoma Mansoni	
Albert J. Kahane, Captain, USAF (MC) and Francisco B. Martin, M.D., Brooklyn, N. Y.	1194
NORMAL PREGNANCIES IN A JUVENILE HYPOTHYROID PATIENT	
Julio Paz-Carranza, M.D., Martin Perlmutter, M.D., and Lowel Prigerson, M.D., Brooklyn, N. Y.	1199
Malformations of the Uterus and Pregnancy	
PREGNANCY IN A NONCOMMUNICATING RUDIMENTARY HORN	
Elmer Gergely, M.D., and Daniel J. Mason, M.D., Brooklyn, N. Y AN UNUSUAL CASE OF RUPTURE OF A PREGNANT RUDIMENTARY HORN OF A BICORNUATE UTERUS	1202
Jack A. Goldman, M.D., and Benjamin Eckerling, M.D., Petach-Tiqvah, Israel	1205
A Robert Pelvis	
Irwin H. Kaiser, M.D., Minneapolis, Minn	1208
Management of Labor	
EVALUATION OF PARAVERTEBRAL LUMBAR SYMPATHETIC BLOCK IN LABOR	
Lucy A. LaSalvia, M.D., Paul S. Copit, M.D., and V. E. Kondon, M.D., Philadelphia, Pa.	1212
GANGRENE AFTER USE OF GAMMA-DIMETHYLAMINO-N-PROPYL PHENOTHI- AZINE HYDROCHLORIDE (PROMAZINE)	
James H. Shell, Jr., M.D., Davis B. McIntyre, Jr., M.D., and James Castellano, M.D., Baltimore, Md.	1219



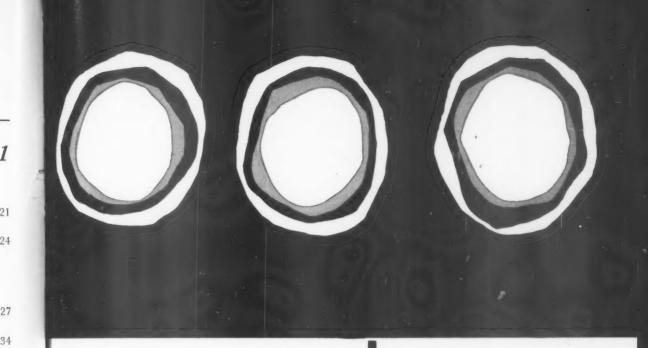
#### continued from page 1

in

thi

Complications of Labor	
SPONTANEOUS DETACHMENT OF THE CERVIX DURING LABOR	
John Garry, M.D., Beverly, Mass	1221
INVERSION OF THE PUERPERAL UTERUS MANAGED BY THE HAULTAIN TECHNIQU	E
Charles L. Easterday, M.D., and Duncan E. Reid, M.D., Boston, Mass	1224
Fetus and the Newborn	
A STUDY OF STAPHYLOCOCCIC COLONIZATION OF POSTPARTUM MOTHERS AND NEWBORN INFANTS	
Thaddeus L. Montgomery, M.D., Robert I. Wise, M.D., Warren R. Lang, M.D., Robert J. Mandle, Ph.D., and MaryAnn Fritz, M.S., Philadelphia, Pa	1227
PRESENTATION AND PROLAPSE OF THE UMBILICAL CORD	
L. M. Norburn, M.B., Ch.B., M.R.C.O.G., Northampton, England	1234
DEMONSTRATION OF CYTOMEGALIC INCLUSIONS IN AUTOLYZED FETAL TISSUE	
Lester F. Belter, M.D., and Marta Camilo, M.D., Richmond, Va	1243
MECONIUM PERITONITIS WITH ASCITES RESULTING IN DYSTOCIA	
Leonard A. Wall, M.D., Kansas City, Mo	1247
Pregnancy Tests	
PRELIMINARY REPORT OF AN ELECTROPLATING TEST OF URINE FOR PREGNANCY	
Walter H. Hartung, Jr., M.D., and Herbert J. DeVauent, E.E., Toledo, Ohio .	1250
GYNECOLOGY	
Ovarian Histology and Physiology	
Ovarian Hilus Cells	
James A. Merrill, M.D., San Francisco, Calif	1258
THE FATE OF THE CORPUS ALBICANS: A QUANTITATIVE APPROACH	
Robert V. Joel, M.D., and Alvan G. Foraker, M.D., Jacksonville, Fla	1272
Surgical Procedures and Complications	1-1-
THE REPAIR OF GENITAL PROLAPSE	
George B. Gibson, M.A., M.A.O., F.R.C.S.(Ed.), M.R.C.O.G., Lurgan, Northern	
Ireland	1275
VASOPRESSIN AS A HEMOSTATIC IN GYNECOLOGIC SURGERY	
Thomas F. Dillon, M.D., New York, N.Y	1285
ABDOMINAL MENSTRUAL FISTULA	
John A. Kirkland, M.D., Chapel Hill, N. C	1292
LYMPHOCYST FORMATION FOLLOWING PELVIC LYMPHADENECTOMY	
James H. Nelson, Jr., Lieutenant (MC) USN, and J. Wilson Huston, Captain (MC) USN	1298
Superior Mesenteric Syndrome Following Pelvic Inflammatory Disease George H. Haddad, M.D., and Wayne H. Decker, M.D., New York, N. Y.	
(Contents continued on Page 4)	

Vol. 78, No. 6, December, 1959. American Journal of Obstetrics and Gynecology is published monthly by The C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Mo. Subscription rates: United States and its Possessions \$15.00, Students \$7.50; Canada, Latin-America, and \$16.00, Students \$8.50; Other Countries \$17.50, Students \$10.00. Single copies \$2.50 postpaid. Entered as Second-Class Matter at Post Office at St. Louis, Mo., under Act of March 3, 1879. Printed in the U. S. A. Copyright © 1959 by The C. V. Mosby Company.



#### in female reproductive disorders

43

47

50

58

72

75

285

292

98

hed ion and osta 3. On the basis of current concepts of the nature of the hypometabolic syndrome, Kupperman et al. state that patients having reproductive disorders associated with this syndrome "may be managed effectively only with liothyronine: the specific hormone replacement therapy."

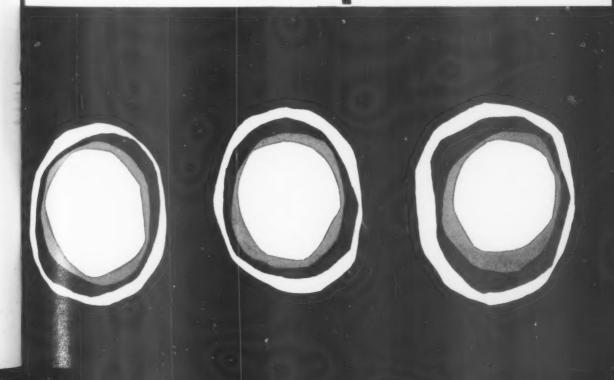
> Fertil. & Steril. 9:26 (Jan.-Feb.) 1958.

## Cytomel\*

5 mcg. & 25 mcg. (scored) tablets

Smith Kline & French Laboratories, Philadelphia

\*T.M. Reg. U.S. Pat. Off. for liothyronine, S.K.F. (L-triiodothyronine or LT3)

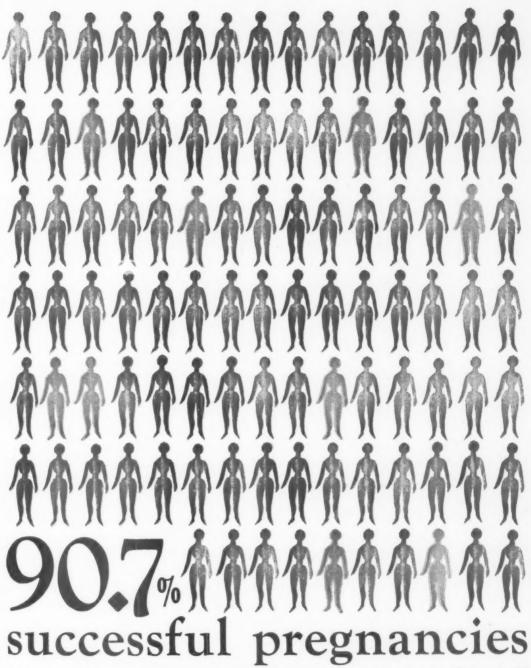


#### contents...



#### continued from page 2

	J. o. P. o.	-
Culdoscopy for Infertility	,	
CULDOSCOPY FOR INFERTILIT		
H. L. Riva, Colonel, MC Breen, Captain, MC, US	T, USA, R. P. Hatch, Captain, MC, USA, and J. L. SA, Washington, D. C.	1304
Diagnostic Procedures		
SIGNIFICANCE OF PERFORMI	NG DUAL SMEAR EXAMINATIONS IN A MASS	
SCREENING SURVEY FOR		
Providence, R. I	ert Fanger, M.D., and Thomas H. Murphy, M.D.,	1309
	MENT: INTRODUCTION OF A NEW TRACHELOTOME	
Louis H. Averbach, M.D.	., Philadelphia, Pa	1312
Vaginitis		
An Evaluation of Routin Vaginalis and Candid	NE CULTURE EXAMINATIONS FOR TRICHOMONAS	
	and Edward Solomons, M.D., Brooklyn, N. Y	1314
A New Agent for the Trea	ATMENT OF VAGINAL CANDIDIASIS	
Bernard Lapan, M.D., Ne	w York, N. Y	1320
Symptoms and Signs of In	traperitoneal Blood	
A STUDY OF THE INJECTION	OF BLOOD INTRAPERITONEALLY INTO WOMEN	
William C. Keettel, M.D., M.D., Iowa City, Iowa .	Kenneth L. Kingsbury, M.D., and Robert C. Hardin,	1324
Tumor of Broad Ligamen	t	
	L NERVOUS SYSTEM OF GYNECOLOGIC INTEREST:	
	A NEURILEMMOMA WITHIN THE RIGHT BROAD	
LIGAMENT MIMICKING	an Ovarian Cyst	
Pittsburgh, Pa	ohn C. Hughes, M.D., and Caesar O. Aldisert, M.D.,	1334
Obstetrical and Gynecolo	gical History	
THE LEGACY OF THE PAST		
Arthur T. Antony, M.D.,	Brooklyn, N. Y	1341
all to the	DEPARTMENT OF CURRENT OPINION	Γ
Clinical Problems		
POSTMENOPAUSAL UTERINE		1347
CARCINOMA OF THE BREAST	AND PREGNANCY · · · · · · · · · · · · · · · · · · ·	1353
	REVIEWS AND ABSTRACTS	
BOOKS RECEIVED FOR REVIEW	W	1358
SELECTED ABSTRACTS · · ·		1358
	CORRESPONDENCE	
CORRESPONDENCE		1368
	INDEX	
INDEX		1373



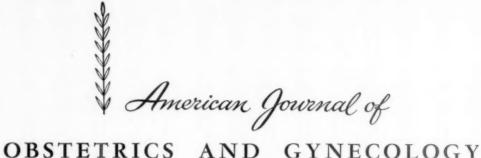
With the addition of Nugestoral to their anti-abortive regimen, Murphy et al.\* brought 78 of 86 habitual aborters to full-term. Nugestoral helps by providing in each daily dose of three tablets 45.0 mg. Progestoral® (ethisterone), 525.0 mg. vitamin C, 487.5 mg. purified hesperidin, 6.0 mg. vitamin K, 10.5 mg. vitamin E. Boxes of 30 and 100.

NUGESTORAL

"Murphy, H. S., et al., Scientific Exhibit, A.M.A., Dec. 1-4, 1959, Dalles, Tonas.

Organon Inc

Organon Inc.
Orange, New Jersey



IN ADDITION TO THOSE LISTED ON THE FRONT COVER, THE JOURNAL IS

THE OFFICIAL PUBLICATION OF THE FOLLOWING SOCIETIES:

NEW YORK OBSTETRICAL SOCIETY OBSTETRICAL SOCIETY OF PHILADELPHIA BROOKLYN GYNECOLOGICAL SOCIETY ST. LOUIS GYNECOLOGICAL SOCIETY NEW ORLEANS GYNECOLOGICAL AND OBSTETRICAL SOCIETY THE OBSTETRICAL AND GYNECOLOGICAL SOCIETY OF MARYLAND CHICAGO GYNECOLOGICAL SOCIETY CINCINNATI OBSTETRICAL AND GYNECOLOGICAL SOCIETY AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY WASHINGTON GYNECOLOGICAL SOCIETY PITTSBURGH OBSTETRICAL AND GYNECOLOGICAL SOCIETY OBSTETRICAL SOCIETY OF BOSTON LOUISVILLE OBSTETRICAL AND GYNECOLOGICAL SOCIETY SEATTLE GYNECOLOGICAL SOCIETY ALABAMA ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS AKRON OBSTETRICAL AND GYNECOLOGICAL SOCIETY KANSAS CITY GYNECOLOGICAL SOCIETY CENTRAL NEW YORK ASSOCIATION OF GYNECOLOGISTS AND OBSTETRICIANS NEW JERSEY OBSTETRICAL AND GYNECOLOGICAL SOCIETY IOWA OBSTETRIC AND GYNECOLOGIC SOCIETY THE TEXAS ASSOCIATION OF OBSTETRICIANS AND GYNECOLOGISTS OKLAHOMA CITY OBSTETRICAL AND GYNECOLOGICAL SOCIETY MEMPHIS OBSTETRICAL AND GYNECOLOGICAL SOCIETY UTAH OBSTETRICAL AND GYNECOLOGICAL SOCIETY ROCHESTER OBSTETRICAL AND GYNECOLOGICAL SOCIETY

ARKANSAS OBSTETRICAL AND GYNECOLOGICAL SOCIETY



ACID TYPES from the Gelusil Family Album

AUNT EFFIE

Aunt Effie was the family's all-out worrier. Things were bad? . . . they'd get worse. Going well? Look out for trouble. Nervous as a cat, she had a stomach to match and only her "soda" to console it.

The years and Aunt Effie have passed, but not the dedicated worriers. Today, though, you can provide lastingly effective pain relief and acid control for *their* nervous stomachs with Gelusil... the antacid adsorbent Aunt Effie should have had.

Especially important to your hospitalized patients . . . Gelusil is all antacid in action . . . contains no laxative . . . does not constipate. Prescribe Gelusil, the choice of modern physicians, for every antacid need.

GELUSIL®
the physician's antacid





#### OBSTETRICS AND GYNECOLOGY

#### Editors

HOWARD C. TAYLOR, JR., Editor in Chief JOHN I. BREWER and ALLAN C. BARNES, Editors LOUIS M. HELLMAN, Abstract and Book Review Editor ROBERT E. HALL, Assistant Editor

> Advisory Committee on Policy 1959

Francis Bayard Carter Andrew Marchetti Daniel G. Morton Newell W. Philpott John Rock Herbert Schmitz

E. Stewart TaylorW. Norman Thornton

#### Advisory Editorial Committee 1959

Albert H. Aldridge Edward Allen Leroy A. Calkins Russell R. de Alvarez R. Gordon Douglas George H. Gardner Louis M. Hellman Carl P. Huber Frank R. Lock

Curtis J. Lund
Harvey B. Matthews
John L. McKelvey
Charles E. McLennan
Joe Vincent Meigs
William F. Mengert
Norman F. Miller
Thaddeus L. Montgomery
Ernest W. Page

Franklin L. Payne Lawrence M. Randall Duncan E. Reid Ralph A. Reis George V. Smith Wm. E. Studdiford Richard W. Te Linde Herbert F. Traut



# Vallestril®

Schneeberg and his associates<sup>2</sup> gave Vallestril to 198 patients with postpartum breast engorgement, pain and lactation. They reported: "The patients ... achieved over-all results ... somewhat better than those in patients receiving 3 mg. of diethylstilbestrol.... Untoward effects, even when large doses were used, were rare. The 'slight bleeding' recorded ... was probably of no significance and was doubtless no more than would have occurred in these individuals without therapy."

Napp, Goldfarb and Massell<sup>3</sup> conducted a controlled study in which 207 postpartum patients received Vallestril, 213 patients were given diethylstilbestrol and 193 patients did not receive hormone therapy. "The stilbestrol treated group showed a significantly greater incidence both of interim bleeding and of hypermenorrhea than did the control or the Vallestril treated groups."

These authors concluded that "Vallestril is a

-avoids most withdrawal bleeding

-minimizes secondary breast symptoms and uterine subinvolution

-"... causes fewer gastrointestinal upsets<sup>1</sup> than does diethylstilbestrol."

superior synthetic estrogen for the suppression of lactation. The low incidence of interim bleeding and of hypermenorrhea constitute a most important characteristic of the drug."

Only two 20-mg, tablets taken daily, for five days, suppress lactation and relieve engorgement and pain. Dosages for indications other than the suppression of lactation are given in Reference Manual No. 7. G. D. Searle & Co., Research in the Service of Medicine.

SEARLE

Council on Drugs: New and Nonofficial Drugs 1958.
 Methallenestril, Philadelphia, J. B. Lippincott Company, 1958, pp. 477-478.

<sup>2.</sup> Schneeberg, N. G.; Perczek, L.; Nodine, J. H., and Perloff, W. H.: Methallenestril, a New Synthetic Estrogen, J.A.M.A. 161:1062 (July 14) 1956.

<sup>3.</sup> Napp, E. E.; Goldfarb, A. F., and Massell, G.: The Parenteral Use of Methallenestril for the Suppression of Lactation. A New Approach, West. J. Surg. 64:492 (Sept.) 1956.

American

Journal of OBSTETRICS GYNECOLOGY

#### EDITORS:

HOWARD C. TAYLOR, JR., Editor in Chief 622 West 168th St., New York 32, 1. Y.

JOHN I. BREWER, Editor 303 East Chicago Ave., Chicago 11, Ill.

ALLAN C. BARNES, Editor 2065 Adelbert Road, Cleveland 6, Ohio

Published by The C. V. Mosby Company 3207 Washington Blvd., St. Louis 3, Mo.

Entered at the Post Office at St. Louis, Mo., as Second-Class Matter.

Published Monthly. Subscriptions may begin at any time.

#### **Editorial Communications**

Submission of Contributions.—Manuscripts should in general be sent to a particular Editor, according to the following plan: If it was read before one of the sponsoring societies or comes from abroad, to Dr. Howard C. Taylor, Jr.; if its source is from the Northeast, to Dr. Allan C. Barnes; if from the South, Middle West, or West, to Dr. John I. Brewer. The contributor may, however, if he wishes, address his manuscript to any Editor of his selection, but the editorial staff reserves the right to reassign papers from any source among themselves. Members of the Advisory Editorial Board may be consulted by the Editors upon suitability of papers submitted for publication.

All articles published in this Journal must be contributed to it exclusively. If subsequently printed elsewhere (except in a volume of Society Transactions) due credit shall be given for original publication. The Editors expect all contributions to conform strictly to this rule.

It is assumed by the Editors that articles emanating from a particular institution are submitted with the approval of the requisite authority.

Neither the Editors nor the publishers accept responsibility from the views and statements of authors as published in their original communications.

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double

of authors as published in their original communications.

Manuscripts.—Manuscripts should be typewritten on one side of the paper only, with double spacing and liberal margins. References should be placed at the end of the article and should conform to the style of the Quarterly Cumulative Index Medicus: viz., name of author, name of periodical, volume, page, and year. Illustrations accompanying manuscripts should be numbered, provided with suitable legends, and marked lightly on the back with the author's name. Authors should indicate on the manuscript the approximate position of tables and text figures.

Illustrations.—A reasonable number of halftone illustrations will be reproduced free of cost to the author, but special arrangements must be made with the Editors for color plates, elaborate tables, or extra illustrations. Copy for zinc cuts (such as pen drawings and charts) must be drawn and lettered in India ink or black typewriter ribbon (when the typewriter is used). Only good glossy photographic prints should be supplied for halftone work; original drawings, not photographs of them, should accompany the manuscript.

Anneuncements.—Announcements of meetings must be received by the Editors at least 214

-Announcements of meetings must be received by the Editors at least 21/4 months before the time of the meeting.

Exchanges.—Contributions, letters, exchanges, reprints, and all other communications relating to the Abstract section of the Journal should be sent to Dr. Louis M. Hellman, State University of New York, College of Medicine, 451 Clarkson Ave., Brooklyn 3, N. Y.

Review of Books.—Books and monographs, native and foreign, on obstetrics, gynecology, and abdominal surgery, will be reviewed according to their merits and the space at disposal. Send books to Dr. Louis M. Hellman, State University of New York, College of Medicine, 451 Clarkson Ave., Brooklyn 3, N. Y.

Reprints.—Reprints of articles must be ordered from the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo., who will send their schedule of prices. Individual reprints of an article must be obtained through the author.

#### **Business Communications**

Business Communications.—All communications in regard to advertising, subscriptions, changes of address, etc., should be addressed to the publishers, The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Mo.

Subscription Rates.—United States and its Possessions \$15.00, Students \$7.50; Canada, Latin-America, and Spain \$16.00, Students \$8.50; Other Countries \$17.50, Students \$10.00, Single copies \$2.50 postpaid. Remittances for subscription should be made by check, draft, post office or express money order, payable to this Journal.

Publication Order.—The monthly issues of this Journal form two semiannual volumes; the index is in the last issue of the volume—in the June and December issues.

Change of Address Notice.—Six weeks' notice is required to effect a change of address. Kindly give the exact name under which a subscription is entered, and the full form of both old and new addresses, including the post office zone number.

Advertisements.—Only products of known scientific value will be given space. Forms close first day of month preceding date of issue. Advertising rates and page sizes will be given on application.

Bound Volumes.—Publishers' Authorized Bindery Service, 5811 West Division Street, Chicago 51, Ill., will quote prices for binding complete volumes in permanent buckram.



## FLORAQUIN® REGIMEN

#### Reverses Vaginal Pathology Toward Normal Physiology—

Basically the Floraquin regimen accomplishes the following three-step restorative action:

- Step 1—Diodoquin® content destroys monilia, protozoa and trichomonads, thereby clearing the way for ...
- Step 2—Acid content helps reestablish the normal pH (3.8 to 4.4) favorable to the regrowth of Döderlein bacilli.
- Step 3—Dextrose and lactose content furnishes essential nutriment to Döder-

Treatment Procedure—Following an initial three to five-day office treatment, the patient is "... issued a prescription for Floraquin vaginal suppositories which she is instructed to insert high into the vagina each evening. On the morning following each application of these suppositories, the patient should take a vinegar water douche.... The treatment continues through the next menstrual period, both the douches and the insertion of the suppositories being continued through the menstrual period."\*

#### Intravaginal Applicator for Simplified Self-Treatment

With this smooth, unbreakable, plastic plunger the tablets may be placed in the vaginal fornices, assuring coating of the entire mucosa as the tablets disintegrate. A Floraquin applicator is supplied with each box of 50 tablets.



Supplied: Powder — bottles of 1 and 8 ounces. Vaginal tablets—boxes of 24 and also boxes of 50 with applicator.

G. D. Searle & Co., Chicago 80, Illinois.

\*Williamson, P.: Trichomonad Infestation, M. Times 84:929 (Sept.) 1956.

SEARLE

Research in the Service of Medicine

### dynamic in toxemia of pregnancy...

#### in single-drug diuresis for simple edema

Through a simple yet dynamic mechanism of action,
DIAMOX controls edema without depleting essential potassium. Gentle diuresis begun early in pregnancy, may preclude more severe toxic states later. One
DIAMOX tablet daily . . . pleasant to take . . . free from gastric and renal irritation.

#### in combined therapy for refractory toxemia

Difficult to reverse once
established, toxemia of
pregnancy may be ameliorated
by aggressive diuresis,
alternating DIAMOX with
chloride-regulating agents.
More efficient than either
agent alone, dual-drug therapy
helps protect serum
electrolyte balance . . . prolong
effective diuresis.

Supplied: Scored tablets of 250 mg., and Vials of 500 mg. for parenteral use.

## DIAMORTO Regulating diuretic HC03 regulating diuretic

LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, New York



safely control the "target symptoms" of emotional stress with the smallest effective dosage (0.25 mg. b.i.d.) of any neuroleptic\* agent

the promise of

# PERMITIL®

Fluphenazine dinydrochioride

nec.

in everyday office practice

# Primer on PERMITIL

#### Why another psychopharmacologic agent?

The ever-expanding role of chemistry in the treatment of mental and emotional problems in this new era of psychopharmacologic drugs is amply attested to by the growing number of rauwolfia, mephenesin, diphenylmethane and phenothiazine derivatives now in clinical use. When one considers the wide range of indications to be treated—from severe psychosis to mild situational stress—it becomes somewhat clearer as to the reason for the number and diversity of drugs available. In addition, improvements and refinements of existing agents are constantly taking place. Drugs tailored to perform a selected, single function are emerging. So it is with Permitti.

#### Why another phenothiazine?

All members of this group contain a phenothiazine nucleus and a side chain attached to the nitrogen atom. Differences in potency are related to specific chemical alterations in these compounds. Clinical evidence demonstrates that the phenothiazines act principally, but to varying degrees, on several subcortical areas of the brain. Thus, certain of these drugs produce sedation and potentiate the action of barbiturates, while others do not; autonomic side effects (such as blurred vision, constipation) are produced by some and not by others; some have been shown to be very effective antiemetic agents. At certain dosage levels, the phenothiazine derivatives also may cause extrapyramidal side effects. These, however, are neuropharmacologic rather than toxic effects and are totally reversible.

Since there is a correlation between the dosage of a phenothiazine derivative and the frequency and the type of side effects it causes, the less of the drug needed to achieve therapeutic results, the less likely are serious side effects. Thus, the lower the effective dosage of a phenothiazine derivative, the lower the incidence of unwanted side reactions and, conversely, the higher the level of therapeutic response.

For these reasons, the search has been unceasing to develop a phenothiazine with an optimum therapeutic ratio.

#### What is a "neuroleptic" agent?

The term "neuroleptic" implies a specific effect of a pharmacologic agent on the nervous system. It refers to a mode of action on specific subcortical areas which strongly influence emotional behavior in contradistinction to hypnotic agents which dull the senses. Neuroleptics achieve control of anxiety symptoms without inducing either somnolence or euphoria. Thus, there is an increase in the patient's capacity to cope with life's problems more successfully. The terms "tranquilizers" and "ataraxics" are descriptively impressive, but they fail to convey what seems pharmacologically unique.

#### Why introduce the term "neuroleptic"?

Because it has a precise psychopharmacologic meaning and is more descriptive of the action of Permitil than any other current term.

#### What is PERMITEL?

PERMITIL is a new anti-anxiety agent of extraordinary potency and effectiveness. Chemically, PERMITIL is 1-(2-hydroxyethyl)-4-[3-(2-triflu oromethyl-10-phenothiazinyl)-propyl]-piperazine dihydrochloride. The structural formula is:

#### Why is PERMITIL unique?

Although Permittl can be broadly classified as a phenothiazine, it exhibits a spectrum of unique effects at unprecedented low dosage—a feature that markedly distinguishes this compound from other anti-anxiety drugs.

#### The Relative Therapeutic Potency of Various Phenothiazines





The potency of each drug was determined by the criteria proposed by Freyhan.<sup>2</sup> These were: (1) the attainable level of psychomotor inhibition, (2) the speed of action, and (3) the dosage required to obtain effective action.

#### What are the distinctive clinical advantages of Permittl.?

Extensive clinical studies have established important psychopharmacologic advantages for Permittle.

- I. The effective dosage of Permitil (0.25 mg, b.i.d.) is the lowest safe dosage of any anti-anxiety agent. Since fractional milligram doses of Permitil usually produce a therapeutic effect, many of the annoying side effects of the other phenothiazines, which are dose-related, occur less frequently or not at all. In fact, any side effects associated with dosage not exceeding 1 mg. per day have been uncommon and transitory. Permitil represents an advance over its predecessors because of its higher level of therapeutic response and low order of side reactions.
- 2. Unlike other phenothiazines, Permitil alleviates symptoms of anxiety, tension, agitation and emotional unrest without depressant effect, impaired alertness or slowed intellectual function. Furthermore, anxiety-induced symptoms of apathy, indifference, listlessness, reduced initiative and chronic emotional fatigue (often refractory to other phenothiazines) frequently respond to administration of Permitil. Thus, a significantly wider spectrum of "target symptoms" amenable to therapy is an outstanding property of Permitil.
- Onset of action is rapid and patients soon become more relaxed and less tense. The patient regains a more confident outlook and normal drive is restored.
- 4. Permittl has an inherently long duration of effect. This makes possible a particularly convenient and easy-to-remember schedule of morning and evening dosage.

#### For what, specifically, is PERMITIL indicated?

PERMITIL is indicated for the control of the "target symptoms" of emotional stress so common in everyday office practice. The basic areas of usefulness for PERMITIL are: (1) behavioral disturbances characterized by anxiety, tension, apprehension and instability, as well as depressive symptoms associated with anxiety states; (2) emotional stress accompanying organic disorders and complicating recovery from, or acceptance of, the underlying condition; (3) chronic disorders in which anxiety and stress are contributing factors, e.g., gastrointestinal dysfunctions, neurodermatitis, asthma, premenstrual tension, arthritis, hypertension and tension headache.

#### Is the dosage schedule, as with many phenothiazine derivatives, complex and complicated?

No. PERMITIL has an inherently long duration of effect so that twice-a-day dosage provides the patient with day and night symptom alleviation. The lowest dose of PERMITIL that will produce the desired clinical effect should be used. The recommended dose for most adults is one 0.25 mg. tablet twice a day. This may be increased to two 0.25 mg. tablets twice a day if required. Total daily dosage in excess of 1 mg. should be employed only in patients with relatively severe symptoms who have had a trial of lower dosages first that were well tolerated but were only partially effective. In such patients, the total daily dose may be increased to a maximum of 2 mg., given in divided amounts. (Dosage for children has not been established.)

#### What about side effects and contraindications to Permittl?

At the recommended dosage of Permitil, side effects have been observed infrequently or not at all. Permitil, as with other phenothiazines, is contraindicated in severely depressed states.

#### How is PERMITEL supplied?

PERMITIL is available as Tablets, 0.25 mg., bottles of 50 and 500.

References: 1. Ayd, F. J.: The current status of major tranquilizers, in press. 2. Freyhan, F. A.: Therapeutic implications of differential effects of new phenothiazine compounds, Am. J. Psychiat. 115:577-585 (Jan.), 1959.

WHITE LABORATORIES, INC., KENILWORTH, NEW JERSEY



#### dual usefulness of



# DESITIN hemorrhoidal SUPPOSITORIES with cod liver oil

hemorrhoids pregnancy



a suppository, such as **Desitin**, reduces straining at the stool by lubricating the anal canal.<sup>1</sup>



conservative treatment is indicated<sup>1-3</sup> for mild to moderate symptoms of simple hemorrhoids, fissures, cryptitis, pruritus ani...in pregnant and other patients.

DESITIN SUPPOSITORIES lubricate, soothe, protect, ease pain, itching... and aid healing (with Norwegian cod liver oil, rich in vitamins A and D and unsaturated fatty acids). Free from drugs which might mask serious rectal disease.

Write for samples and literature1-3

**DESITIN** CHEMICAL COMPANY

812 Branch Ave., Providence 4, R. I,



Improved molecular structure! Higher sodium chloride excretion!

SALUTON TABLETS

30% MORE SODIUM EXCRETION than maximally effective parenteral dosage of meralluride

62% MORE SODIUM EXCRETION than maximally effective oral dosage of chlorothiazide

. with less risk of potassium and bicarbonate depletion

serum electrolyte changes , with no significant

Bristo

A RECORD OF PROGRESS

FIRST - chlorothiazide

NEXT — hydrochlorothiazide

THEN — flumethiazide

NOW - sustained-action hydroflumethiazide 'Bristol'

ent sustained diuresis



REFERENCES:

communication.

communication.

tion.

Dube, A. C., Van Duyn County Hospital, Onondaga, N. Y.: Personal communica-

Ford, R. V., Nickell, J., and Dennis, E. W.: Ant. Med. & Clin. Ther. 6:461, 1959.

3. Fuchs, M., Hahnemann Medical College, Philadelphia: Personal communication.

Hudson, R., Meyer Memorial Hospital, Buffalo, N. Y.: Personal communication.

5. Meilman, E., Long Island Jewish Hos-pital, New Hyde Park, N. Y.: Personal

# stained-action hydroflumethiazide 'Bristol

#### linical research findings

- Effective dose 50 mg. per day.<sup>1-6</sup>
- Prompt sodium excretion, with "a duration of at least 18 hours."2
- 30% more natriuresis than parenteral meralluride -

62% more than oral chlorothiazide.1

- Less potassium and bicarbonate excretion or pH change than with chlorethiazide or hydrochlorothiazide.1
- "No significant serum electrolyte changes."2
- Continued effectiveness with prolonged use.1,2,4,5,8
- Well tolerated. 1-6

#### INDICATIONS:

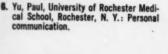
SALURON is indicated for the treatment of salt and water retention associated with cardiac or renal insufficiency, hepatic cirrhosis, pregnancy, premenstrual syndrome, or steroid administration.

#### DOSAGE:

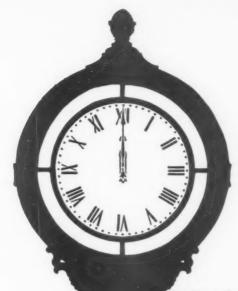
Usual dose one tablet on arising. Some patients respond to as little as 25 mg. per day; but doses as high as 400 mg, may be used. Ideally, the dosage should be adjusted to the individual patient's need, so that effective diuresis is produced with the minimal dose.

#### SUPPLY:

Scored 50 mg. tablets of sustained-action hydroflumethiazide; bottles of 50. Comprehensive information on administration, dosage and precautions on pack age insert, or available on request.







keeping appetite in check around the clock **PRFI IIDIN**°

**ENDURETS** 

prolonged-action tablets

New long-acting PRELUDIN ENDURETS offer you a new method...a more convenient method...of administering this well-established, reliable appetite-suppressant. The new ENDURETS form virtually eliminates the vexing problem of the forgotten dose because... just one PRELUDIN ENDURET taken in the morning generally curbs the appetite throughout the day.

PRELUDIN ENDURETS afford greater convenience for your patient... added assurance to you that medication is being taken as prescribed.

PRELUDIN® (brand of phenmetrazine hydrochloride)
ENDURETS, r.m. Each ENDURETS prolonged-action tablet
contains 75 mg. of active principle.
PRELUDIN is also available as scored, square pink

tablets of 25 mg. for 2 to 3 times daily administration.

Under license from C. H. Boehringer Sohn, Ingelheim.

INDURETS IS A GEIGY TRADEMARK

**GEIGY** 

ARDSLEY, NEW YORK

es of 50. s on pack

othiazide.

th chloro

othiazide.

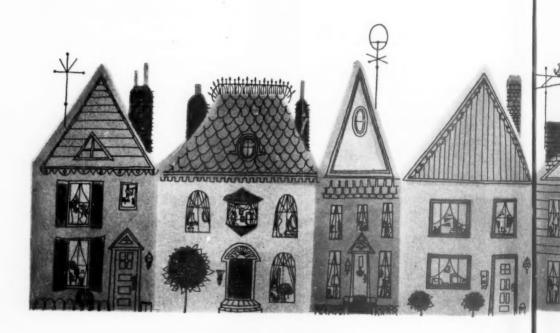
menstrual

ge should sis is pro-

YORK

66But, Doctor,

I just can't
swallow a lot of
tablets 99



## 66 Little mother, just ONE

tablet stops morning sickness (you take it at bedtime) 99

> The formula tells why Bonadoxin quickly stops nausea and vomiting of pregnancy in 9 out of 10 cases.\*

Each tiny Bonadoxin tablet contains: Meclizine HCI (25 mg.) for antinauseant action
Pyridoxine HCI (50 mg.) for metabolic replacement

More than 60,000,000 tablets prescribed and taken. Toxicity low, tolerance excellent. In bottles of 25 and 100. Usual dose: one tablet at bedtime; severe cases may require another on arising. See PDR, p. 779.

Bonadoxin also effectively relieves nausea and vomiting associated with: anesthesia, radiation sickness, Meniere's syndrome, labyrinthitis, cerebral arteriosclerosis and motion sickness.



New York 17, New York Division, Chas. Pfizer & Co., Inc. Science for the World's Well-Being



For infant colic, try antispasmodic Bonadoxin Drops... stop colic in 7 out of 8 cases.\* Each cc. contains: Meclizine 8.33 mg. / Pyridoxine 16.67 mg.

See PDR, p. 779.

\*Bibliography available on request.





## 27 pounds lost in 19 days; ascites and

 RECORD OF TREATMENT (At a leading New York City hospital. Photos used with permission of the patient.)

 Date
 3/3
 3/4
 3/5
 3/6
 3/7
 3/8
 3/9
 3/10
 3/11
 3/12
 3/13
 3/14
 3/15
 3/16
 3/17
 3/18
 3/19
 3/20
 3/21
 3/22
 3/23

 Weight (pounds)
 178
 176
 170
 169
 167
 159
 158
 158
 157
 153
 155
 156
 154
 153
 153
 151
 149

 Rx
 M\*
 Esidrix 50 mg. b.i.d.

<sup>\*</sup>Mercurial diuretic



# (hydrochlorothiazide CIBA)

pre-eminently effective whenever diuresis is desired

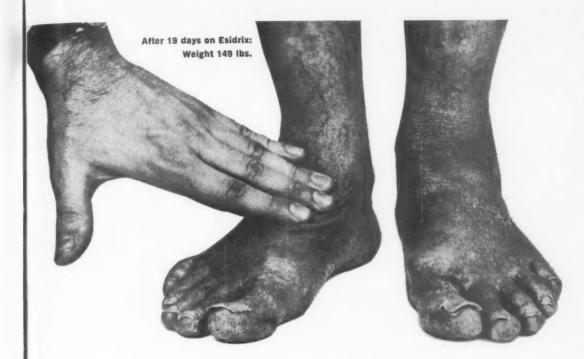
Indicated in: congestive heart failure . . . nephrosis and nephritis . . . toxemia of pregnancy . . . premenstrual edema . . . edema of pregnancy . . . steroid-induced edema . . . edema of obesity

Supplied: Esidrix Tablets, 25 mg. (pink, scored) and 50 mg. (yellow, scored); bottles of 100 and 1000.





Am. J. Obst. & Gynec.



# pedal edema reduced with Esidrix

H. K., 44 years old, was admitted to the hospital on 3/3/59 with complaints of swollen abdomen, swelling of both legs and exertional dyspnea. These symptoms had been intensifying over a three-week period. The patient's history included heavy drinking since the age of 18, and one prior admission to the hospital in 1954 with ascites and pedal edema. Diagnosis, at that time, was Laennec's cirrhosis, and the patient responded well to a regimen of diuretics, salt restriction and multivitamins. There was no recurrence up to that leading to his current admission.

Clinical findings worthy of note: Eyes — conjunctivae and sclerae slightly icteric. Chest—diaphragm elevated. Abdomen — girth enlarged, definite fluid wave. Liver palpated 4 fingerbreadths below the costal margin; no other palpable viscera. Extremities—pedal 'edema (4+).

The patient is well developed and not in acute distress. Blood pressure, 140/80 mm. Hg; pulse, 112/min.; respiration, 20/min. Impression: Laennec's cirrhosis—decompensated.

Treatment: Mercurial diuretic on 3/3 and 3/4, followed by Esidrix, 50 mg. b.i.d., from 3/5 to 3/23 when patient signed out of hospital. Esidrix induced copious diuresis resulting in almost complete disappearance of edema.

2/2714MK

nec.

nd

patient.)

51 149

December, 1959

Page 23

Roche Laboratories announces

# Tigan

to stop as well as prevent nausea and vomiting of pregnancy

A safe, completely different antiemetic antinauseant

available in oral, parenteral and suppository forms.

## for a pregnancy unmarred by "morning sickness," uncomplicated by hyperemesis gravidarum

TIGAN is equal in effectiveness to the most potent antiemetics. It not only safely prevents "morning sickness," but usually stops even severe, intractable vomiting.<sup>1</sup>

#### Acts at the CTZ-like the most potent antiemetics

Tigan blocks emetic impulses at the chemoreceptor trigger zone (CTZ),<sup>2</sup> a medullary structure which activates the vomiting center. To this extent, Tigan is like the most potent antiemetic agents—the phenothiazines.<sup>3</sup>

#### Safe-without the side effects of the antihistamines

In extensive clinical studies, 1.4-6 Tigan has demonstrated a virtually complete absence of side effects. It has no sedative properties; 4-6 therefore, patients receiving Tigan may drive an automobile without the hazard of drowsiness, and carry on their household activities without being troubled by added lethargy or sleepiness.

#### Safe-without the risks of the phenothiazines

The mode of antiemetic action is the only similarity between Tigan and the phenothiazines. Chemically and pharmacologically, they are completely unrelated.<sup>2</sup> Tigan has no tranquilizing properties, hypotensive action, supramedullary effects, extrapyramidal tract stimulation or hepatic toxicity.<sup>1,4-6</sup> In laboratory findings there has been not one reported instance of abnormality due to Tigan.<sup>1,4-6</sup>

#### No known contraindications

There are no known contraindications, no special precautions to complicate Tigan therapy.

# Ilgan

no known contraindications...no sedative properties...no tranquilizer side effects

Dosage: Usual recommended adult dose of Tigan is 200 mg initially, to be followed by doses of 100-200 mg q.i.d. as required. In nausea and vomiting of pregnancy satisfactory control is usually achieved by an initial dose of two capsules (200 mg) immediately upon awakening. For the patient whose nausea and vomiting is not confined to the morning hours, supplemental doses of 100 mg should be given throughout the day at intervals of three to four hours.

Available: Capsules, 100 mg, blue and white; bottles of 100 and 500. Ampuls, 2 cc (100 mg/cc); boxes of 6 and 25. Pediatric Suppositories, 200 mg; boxes of 6.

#### References:

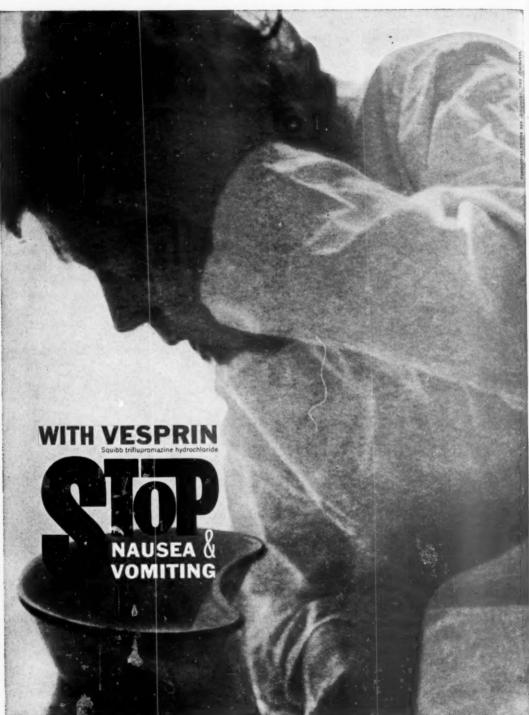
- 1. Reports on file, Roche Laboratories.
- W. Schallek, G. A. Heise, E. F. Keith and R. E. Bagdon, J. Pharmacol. & Exper. Therap., 126:270, 1959.
- L. S. Goodman and A. Gilman, The Pharmocological Basis of Therapeutics, ed. 2, New York, The Macmillan Company, 1956, p. 1066.
- 4. O. Brandman, to be published.
- I. Roseff, W. B. Abrams, J. Kaufman, L. Goldman and A. Bernstein, J. Newark Beth Israel Hosp., 9:189, 1958.
- W. B. Abrams, I. Roseff, J. Kaufman, L. Goldman and A. Bernstein, to be published.

#### ROCHE LABORATORIES



Division of Hoffmann-La Roche Inc. Nutley 10, N.J.

TIGAN® Hydrochloride - 4-(2-dimethylaminoethoxy)-N-(3,4,5-trimethoxybenzoyl)benzylamine hydrochloride ROCHE®



Dosage: Intravenous, 5 to 12 mg. / Intramuscular, 5 to 15 mg. / Oral prophylaxis, 20 to 30 mg. daily / Supply: Tablets, 10, 25, and 50 mg. bottles of 50 and 500 / Emulsion, 30-cc. dropper bottles and 120-cc. bottles (10 mg./cc.) / Parenteral Solution, 1-cc. multiple dose vial (20 mg./cc.) / 10-cc. multiple dose vial (10 mg./cc.) / Vesprin Injection Unimatic (15 mg. in 0.75 cc.)

Vesprin/the tranquilizer that fills a need in every major area of medical practice/ SQUIBB anxiety and tension states, pre- and postoperative tranquilization, alcoholism, and obstetrics

в

Squibb Quality - the Priceless Ingredient wor

age and chi ma

70

A'I

BI BA

Work grow required uals mia grow nize hem dur

exc ple and wel bet

tor

FOR Iron (Mar Thi Rib Vita

> Nic Pyr

> Par

Liv Ric Inc

SU

women of childbearing age... and growing children... when the children is a second children is a second children...

# OVERDRAWN AT THE BLOOD BANK

Women of menstrual age and growing children have higher iron requirements than other individuals. Hence iron-deficiency anemias occur most often in these groups. Many clinicians recognize that most women need a hematinic for six weeks each year during reproductive years.

Livitamin, with peptonized iron and B complex, offers an excellent formula to restore depleted iron reserves in both adults and children. Peptonized iron is well absorbed and stored, and better tolerated than ferrous sulfate. B complex and other factors provide nutritional support.



	1 .11 -1
Sharles Smith	19 19 89 100 fg
hed and	BOLEAR'S
1882	Hulley
	beerfee Emith bef suf





## LIVITAMIN

FORMULA: Each fluidounce contains:

Iron peptonized 420 mg. (Equiv. in elemental iron to 71 mg.)

Manganese citrate, soluble 158 mg.

Thiamine hydrochloride 10 mg.

Thiamine hydrochloride 10 mg.
Riboflavin 10 mg.
Vitamin B<sub>12</sub> Activity 20 mcg.
(Derived from Cobalamin conc.)

Nicotinamide 50 mg.
Pyridoxine hydrochloride 1 mg.
Pantothenic acid 5 mg.
Liver fraction 1 2 Gm.
Rice bran extract 1 Gm.
Inositol 30 mg.

60 mg.

SUPPLIED IN LIQUID OR CAPSULE.

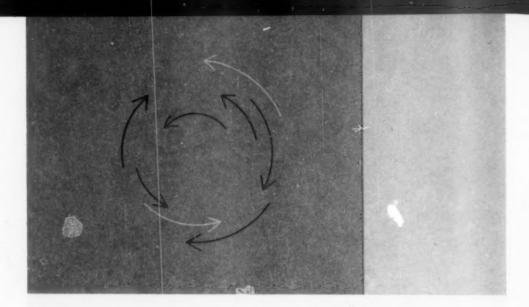
Choline

iec.

with Peptonized Iron

The S.E. ASSENGILL Company

BRISTOL, TENNESSEE . NEW YORK . KANSAS CITY . SAN FRANCISCO



Livitamin assures patient acceptance because it is highly palatable. Peptonized iron provides a virtually predigested form of iron. Recent studies\* show peptonized iron has these advantages:

- Rapid response in iron-deficiency anemias
- Non-astringent
- Absorbed as well as ferrous sulfate
- Better gastric toleration than ferrous sulfate
- Less constipating than ferrous sulfate



... the preferred hematinic

\*Keith, J.H.: Utilization and Toxicity of Peptonized Iron and Ferrous Sulfate, Am. J. Clin. Nutrition 1:35 (Jan.-Feb., 1957).

The S. E. MASSENGILL Company BRISTOL, TENNESSEE

NEW YORK . KANSAS CITY . SAN FRANCISO

#### In the menopause... transition without tears



#### Milprem promptly relieves emotional distress with lasting control of physical symptoms

# Milprem<sup>e</sup>

Supplied in two potencies for dosage flexibility: MILPREM-400, each coated pink tablet contains 400 mg. Miltown (meprobamate) and 0.4 mg. conjugated estrogens (equine). MILPREM-200, each coated old-rose tablet contains 200 mg. Miltown and 0.4 mg. conjugated estrogens (equine).

Both potencies in bottles of 60.

Literature and samples on request.

In minutes, Milprem starts to ease anxiety and depression. It relieves insomnia, relaxes tense muscles; alleviates low back pain and tension headache. As the patient continues on Milprem, the replacement of estrogens checks hot flushes and other physical symptoms.

Easy dosage schedule: One Milprem tablet t.i.d. in 21-day courses with one-week rest periods; during the rest periods, Miltown alone can sustain the patient.



WALLACE LABORATORIES, New Brunswick, N. J.

CHP-9224-09

December, 1959

Page 29

Bright new star

in the antibacterial firmament

# the first nitrofuran effective orally

in systemic bacterial infections

# ATTARUR. brand of furaltadone

Effective clinically in upper respiratory infections, pneumonias, soft tissue infections, bacteremia/septicemia, osteomyelitis, wound infections and pyodermas.

Effective in vitro against the following organisms (isolated from clinical infections listed above):

Organism	Sensitive	Resistant	% Sensitive
Staphylococci*	181	1	99.4
Streptococci	65	1	98.5
D. pneumoniae	14	0	100.0
Coliforms	34	3	91.8
Proteus	5	5	50.0
A. aerogenes	8	0	100.0
Ps. aeruginosa	5	4	55.5

<sup>\*</sup>Includes many strains resistant to antibiotics.

As with all nitrofurans in years of extensive clinical use, there is little or no development of bacterial resistance with ALTAFUR.

NITROFURANS—a unique class of antimicrobials—neither antibiotics nor sulfonamides

EATON LABORATORIES, NORWICH, NEW YORK



# appreciably less with...FERMALOX

**Uncoated Buffered Ferrous Sulfate** 

HIGHER ABSORPTION-LOWER DOSAGE

When Fermalox is prescribed in anemia "satisfactory clinical response is obtained with 44% of U.S.P. dosage." Uncoated Fermalox tablets disintegrate rapidly making more iron available for immediate absorption in the duodenum producing increased utilization.

Gastric irritation is virtually eliminated with Fermalox due to the buffering action of Maalox. Many patients who can't take iron can take Fermalox.

Each FERMALOX tablet contains: Ferrous sulfate 200 mg.; MAALOX-Rorer (Magnesium-aluminum hydroxides) 200 mg.

Dosage: 2 tablets daily; often may be reduced to 1 tablet daily after 15 days.

Offered: Bottles of 100 tablets at prescription pharmacies.

1. Price, A.H. et al.: J.A.M.A. 167:1612, 1958.



WILLIAM H. RORER, INC.

Philadelphia 44, Pa.

# NOW...IN CERVICITIS VAGINITIS

stop the torment...destroy the cause

new

suppositories

provide all the proven effectiveness of AVC Improved Cream in a completely new suppository form. The gelatin capsule disintegrates in 8-10 minutes; the AVC then spreads rapidly.

new effectiveness

suppositories

have proved effective in a wide variety of vaginal conditions.<sup>1,2,9,11,12</sup> The "CURE" rate with AVC Improved is consistently high.<sup>2-6,0,19</sup> Irritation and itching are relieved, discharge and odor are eliminated and the causative pathogens destroyed.

new convenience 1.7,5,11,18

IMPROVED

suppositories

may be carried in the purse or pocket. They are ideal for use away from home, at work or while travelling. Easily inserted with or without applicator. Appearance and touch, not greasy or sticky, encourage patient cooperation and acceptance.

IMPROVED

suppositories

Administration: One suppository inserted intravaginally, twice daily.

Supplied: Box of 12 suppositories with applicator.

References: 1. Peikes, I. L.: Journal-Lancet 79:368, 1959. 2. Cacciarelli, R. A.: J. M. Soc. New Jersey 46:87, 1949. 3. Cortese, J. T.: Clin. Med. 2:45, 1955. 4. Dill, L. V., and Martin, S. S.: M. Ann. District of Columbia 17:389, 1948. 5. Hensel, H. A.: Postgrad. Med. 8:293, 1950. 6. Angelucci, H. M.: Am. J. Obst. & Gynec. 50:336, 1945. 7. Cicalese, G.: Personal communication. 8. Horoschak, A., and Horoschak, S.: J. M. Soc. New Jersey 43:92, 1946. 9. Crisp, W. E.: Personal communication. 10. Parks, J.: M. Ann. District of Columbia 12:175, 1943. 11. Kroger, W. S.: Personal communication. 12. Peikes, I. L.: In press.

Products of Original Research



THE NATIONAL DRUG COMPANY Philadelphia 44, Pa.

AFTER FIRST STAGE

A SINGLE INJECTION

AFTER DELIVERY

LACTATION SUPPRESSED
NO COMPLICATIONS





# **DELADUMONE 2X**

CONVENIENT OPTIMALLY BALANCED LONG-ACTING

MORE EFFECTIVE THAN THE ORAL MEDICATION

NOTABLY FREE FROM UNWANTED EFFECTS Especially designed for convenient suppression of lactation, Deladumone 2X contains the same "optimally balanced, long-acting combination" of testicular and follicular hormones provided by Deladumone in double the potency. "...[Deladumone] compares very favorably with other preparations in use for the inhibition of lactation and has the additional advantage of requiring only a single intramuscular injection." 2

"When employed in an adequate dosage at the proper time, the need for analgesics to control the breast symptoms is practically eliminated.... The use of Deladumone appears to essentially eliminate the undesirable withdrawal reaction or secondary breast engorgement that occasionally follows the cessation of oral medication."

"... the balance of the hormonal components in DELADUMONE is such that it is possible to administer this preparation in a sufficiently large dose to prevent lactation without affecting the involution of the uterus, the character of the lochia, or the restoration of normal ovarian function."

Supply: Each cc. of Deladumone 2X provides 180 mg. testosterone enanthate and 8 mg. estradiol valerate dissolved in sesame oil. Vials of 2 cc.

**Dosage:** 2 cc. given as a single intramuscular injection preferably at the end of the first stage of labor or else *immediately* upon delivery.

1. Lo Presto, B., and Caypinar, E. Y.: J.A.M.A. 169:250 (Jan.) 1959. 2. Stein, W. W.: Am. J. Obst. & Gynec. 76:108 (July) 1958. 3. Watrous, J. B. et al.: J.A.M.A. 169:246 (Jan.) 1959.

SQUIBE



Squibb Quality - the Priceless Ingredient

\*DELADUMONE\*® IS A SQUIBB TRADEMARK

# CHELATED FOR MORE EFFICIENT ORAL



■ outstandingly free from g.i. irritation ■ does not stain teeth [when given as a liquid] ■ can be taken any time — between meals without irritation, or at mealtime without impaired utilization ■ compatible with ulcer medication, and does not cause added irritation ■ safest iron to have in the home because of chelate-controlled absorption ■ and — clinically confirmed as an effective hematinic [Franklin et al.: J.A.M.A. 166:1685, 1958]

CEE - RON

CHELATED the new way to give oral iron

Brand of Iron Choline Citrate\*

Tablets — 1 tablet t.i.d. furnishes 120 mg. iron
Pediatric Drops — 1 cc. furnishes 25 mg. iron
Liquid — 1 tsp. (5 cc.) furnishes 50 mg. iron
also: CHĒL-IRON PLUS Tablets — chelated iron plus B<sub>12</sub>,
folic acid, other B vitamins, and C.



(Kinney)

KINNEY & COMPANY, INC. . COLUMBUS, INDIANA



"Chelate" describes a chemical structure in which metallic ions are "encircled" and their physicochemical properties thereby altered. Chelated iron (as iron choline citrate\*) is unusually soluble; nonionizable; not precipitated by variations in g.i. tract pH, protein, phosphate, or alkali; yet is readily available for hemopoiesis on physiologic demand.

♥U. S. PAT. 2,575,611

For the first time

#### CONVENIENCE and ECONOMY

for that all-important first dose of broad-spectrum antibiotic therapy

New

#### TERRAMYCIN:

brand of oxytetracycline

# INTRAMUSCULAR SOLUTION

Initiation of therapy in minutes after diagnosis with new, ready-to-inject Terramycin Intramuscular Solution provides maximum, sustained absorption of potent broad-spectrum activity.

...and for continued, compatible, coordinated therapy

#### COSA-TERRAMYCIN

oxytetracycline with glucosamine

#### CAPSULES

Continuation with oral Cosa-Teframycin every six hours will provide highly effective antibacterial serum and tissue levels for prompt infection control.

The unsurpassed record of clinical effectiveness and safety established for Terramycin is your guide to successful antibiotic therapy.

#### Supply:

Terramycin Intramuscular Solution\*
100 mg./2 cc. ampules 250 mg./2 cc. ampules

Cosa-Terramycin Capsules 125 mg. and 250 mg.

Cosa-Terramycin is also available as: Cosa-Terramycin Oral Suspension – peach flavored, 125 mg./5 cc., 2 oz. bottle

Cosa-Terramycin Pediatric Drops – peach flavored, 5 mg./drop (100 mg./cc.), 10 cc. bottle with plastic calibrated dropper

Complete information on Terramycin Intramuscular Solution and Cosa-Terramycin oral forms is available through your Pfizer Representative or the Medical Department, Pfizer Laboratories.

Contains 2% Xylocaine (lidocaine), trademark of Astra Pharmaceutical Products, Inc.

PFIZER LABORATORIES, Division, Chas. Pfizer & Co.

Pfizer Science for the world's well-beingm

Brooklyn 6, N. Y.



December, 1959

\*IN THE TREATMENT OF PRE-ECLAMPSIA

pper

entative

Page 37

# FOR ANXIETY\_ particularly when expressed as apathy, listlessness and emotional fatigue



#### TYPICAL PRESENTING SYMPTOMS

loss of normal drive inability to concentrate or work effectively indecisiveness irritability crying spells insomnia anorexia vague fears undue preoccupation with somatic complaints wide swings of mood generalized discomfort headaches dizziness palpitations hyperventilation epigastric distress

## NEW

# Img. STELAZINE\* TABLETS

'Stelazine' is unique because it not only relieves agitation and tension, but also relieves apathy listlessness and emotional fatigue resulting from anxiety states.

Other noteworthy characteristics of 'Stelazine', brought out in clinical studies in over 12,000 patients, are:

- \* may be effective when other agents fail
- \* side effects usually slight and transitory
- \* fast therapeutic response with very low doses
- \* convenient b.i.d. administration

"THE INDIFFERENCE WHICH OCCURS COMMONLY WITH [MOST] OTHER TRANQUILIZERS WAS ABSENT."

This observation about 'Stelazine' points to what may be one of the most important and distinguishing characteristics of the drug-that is, 'Stelazine', while relieving emotional distress, does not "tranquilize" your patients out of normal activity or normal aims.

AVAILABLE for use in everyday practice—1 mg. tablets, in bottles of 50 and 500. Literature available on request. Smith Kline & French Laboratories, Philadelphia.

REFERENCES: 1. Gearren, J.B.: Dis. Nerv. System 20:66 (Feb.) 1959. 2. Margolis, E.J.; Pauley, W.G.; Cauffman, W.J and Gregg, P.C.: Scientific Exhibit at the 12th Clinical Meeting of the American Medical Association, Minneapolis, Minn., Dec 2-5, 1958. 3. Phillips, F.J., and Shoemaker, D.M.: ibid. 4. Ayd, F.J., Jr.: Clin. Med. 6:387 (Mar.) 1959.

\*Trademark

SMITH KLINE & FRENCH

leaders in psychopharmaceutical research

# Imferon

#### INTRAMUSCULAR IRON-DEXTRAN COMPLEX

corrects and prevents iron deficiency in blood and marrow

**PEDIATRICS:** "IMFERON has the advantage of safe and easy administration; treatment is completed in a few days and is not influenced by feeding problems."

**OBSTETRICS:** "...we have been able to raise hemoglobin levels of 7 or 8 Gm. to normal figures within a few weeks...."

CHRONIC BLOOD LOSS: IMFERON "... is also to be preferred to blood transfusions for correcting the effects of chronic blood loss. The risk of transfusion reactions is avoided, as well as the dangers of contamination and sensitization. Besides improving the anemia, iron stores will be replenished..."

**GERIATRICS:**A 66-year-old woman with recurrent gastrointestinal bleeding for over six years [two abdominal explorations, source undiscovered] "...has been maintained at a comfortable blood level for over nine months on intramuscular iron injection, with greatly reduced transfusion requirement."

**SUPPLIED:** 2-cc. and 5-cc. ampuls; 10-cc. multiple-dose vials. There are 50 mg. of elemental iron per cc.

(1) Wallerstein, R. O., and Hoag, M. S.: J.A.M.A. 164:962 (June 29) 1957. (2) Eastman, N. J.: Current M. Dig. 25:55 (Jan.) 1958. (3) Koszewski, B. J., and Walsh, J. R.: Am. J. M. Sc. 235:523 (May) 1958. (4) McCurdy, P. R.; Rath, C. E., and Meerkrebs, G. E.: New England J. Med. 257:1147 (Dec. 12) 1957.

48659



### PROVEN EFFECTIVE FOR THE TENSE AND **NERVOUS PATIENT**



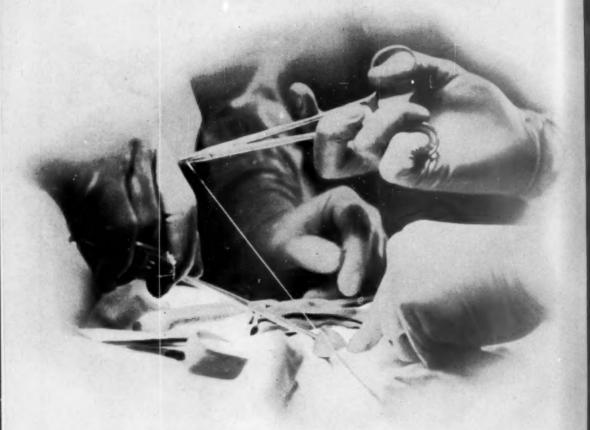
There is perhaps no other drug introduced in recent years which has had such a broad spectrum of clinical application as has meprobamate.\* As a tranquilizer, without an autonomic component in its action, and with a minimum of side effects, meprobamate has met a clinical need in anxiety states and many organic diseases with a tension component. 99

Krantz, J. C., Jr.: The restless patient - A psychologic and pharmacologic viewpoint. Current M. Digest 25:68, Feb. 1958.

nec.

the original meprobamate, discovered and introduced by

WALLACE LABORATORIES, New Brunswick, N. J.



# Premedication without respiratory or circulatory depression

... and with 5 other advantages

PHENERGAN offers unmistakable aid to surgeon, anesthesiologist, and nurse. Proved in many thousands of patients, premedication with Phenergan curbs fear and excitement, prevents nausea and vomiting, facilitates anesthesia, reduces the requirement for depressant anesthetic and analgesic agents, and counteracts sensitivity reactions. All this without producing depression of the vital functions.

#### PHENERGAN® HYDROCHLORIDE

Promethazine Hydrochloride, Wyeth

Wyeth

Bhiladelphia 1 Pa

INJECTION
TABLETS
SYRUP
SUPPOSITORIES

TO FIT YOUR PATIENT...

NEW...

ORTHO® Arcing Spring Diaphragm





forms a perfect are easy to insert... deal for the normal and difficult to fit patient.

ORTHO® Diaphragm (Coil Spring)





flexes in all planes - adapts readily to irregular contours of the vagina...

ORTHO"-WHITE Diaphragm (Flat Spring)





Pleases in one plane—inserts easily, needs no introducer.

A COMPLETE CHOICE





postpartum

patient distress can be prevented...

#### COZYME TH

(d-pantotneny) alcohol. Travenol)

#### A Routine Procedure for the Early Resumption of Postpartum Intestinal Activity

- effectively prevents and corrects abdominal distention . . . and retention of flatus and feces
- restores normal peristaltic activity, physiologically

because COZYME supplies the active molecular component of coenzyme A—pantothenic acid—which is essential in the formation of acetylcholine, the chemical mediator of nerve impulse transmission governing intestinal motility.

Supplied: COZYME 10 ml. multiple dose vial containing 250 mg. per ml. of *d*-pantothenyl alcohol with 0.45% Phenol added as preservative. COZYME 2 ml. single dose vial containing 250 mg. per ml. of *d*-pantothenyl alcohol. 25 vials per carton.

#### TRAVENOL LABORATORIES, INC.

Pharmaceutical Products Division of Baxter Laboratories Inc. Morton Grove, Illinois

licine 6:791-796 (May) 1959. Haycock, C. E.; Davis, W. A., and Morton, T. V.: Am. J. Sure. 97-78 (One.) 1959. Stone, M. L.; Schlussel 6:101-194 (Feb.) 1959. Schulte, F.: Deutsche med. Wchnschr. 80: 188-1191, 1957. Frazer, W. A.; Flowe, B. H., and Anlyan, W. G.: J. A. d. Padilla, J.: To be published. Warlitz, H.: Zentralbi. Chir. 80:1686-1688, 1955. Sclausero G.: Gazz. med. ital. 114:291-293 (Dec.) 1955. Felten, Sazz. med. ital. 116:159-161 (April) 1957. Zutelman, E.: Semana med. 103:688, 1953. Lamphler, T. A.: To be published. Wager, N.: To be published. C.: Minerva med. 46:1610-1612, 1955. Jurgens, R., and Pfaltz, H.: Ztschr. Vitamin- Ho mon- u. Fermentforsch. 3:243-269, 1944. Banerji, T.

Why should I use

KANTREX® Injection\*

when there are
so many other
antibiotics available?

Because Kantrex Injection is bactericidal to a wide variety of organisms, including many that are highly resistant to the other antibiotics<sup>3,4,10,12,13,17,18,20,21,23,24,25,27,30,33,35,37</sup>

-organisms such as Staph. aureus, Staph. albus, A. aerogenes, E. coli, H. pertussis, K. pneumoniae, Neisseria sp., Shigella, Salmonella and many strains of B. proteus.

But if I use Kantrex Injection, won't that help make bacteria resistant to it also?

Next page, please .....

\*Kanamycin sulfate injection (Bristol)

rion of

per carton.

ES, INC.

ed.

e Early

orrects and es

activity,

enzyme

mediator on

of

tiple er ml. 0.45%

W. G.: J.A.

Banerji, T.

- Q But if I use Kantrex Injection, won't that help make bacteria resistant to it also?
- A very good question, but it is reassuring to note that in almost two years of clinical use of Kantrex for the treatment of infections for which it is recommended, the emergence of Kantrex-resistant bacterial populations has not been a problem.
- Q My impression is that Kantrex is just another neomycin. Isn't that so?
- A Indeed not. The only thing Kantrex and neomycin have in common is a similar antimicrobial spectrum. Otherwise, they're very different: they have different chemical structures; the toxicity of Kantrex is "much less than that of neomycin" and clinically, Kantrex Injection is practical for systemic administration routinely, while neomycin is not.
- Q You mean that Kantrex Injection doesn't have the nephrotoxicity of neomycin?
- A Precisely. It's true that when Kantrex Injection is used, urinary casts even slight albuminuria or microscopic hematuria may appear, especially in poorly hydrated patients, but this does not reflect any progressive damage to the kidneys. These signs promptly disappear on adequate hydration or termination of therapy.
- Q Then why do you recommend reduced dosage in patients with renal impairment?
- A Because renal impairment causes an excessive accumulation of Kantrex in the blood and tissues, when usual doses are administered. Since Kantrex Injection is excreted entirely by the kidneys, renal impairment leads

to unnecessarily high and prolonged blood levels; and such excessive concentrations increase the risk of ototoxicity.

- Q Is that why we see reports of patients developing hearing loss during Kantrex Injection therapy?
- A Yes. A study of the few reported cases in which patients have suffered impaired hearing will show that in every instance they had pre-existing or concurrent renal impairment, yet received usual or excessive doses of Kantrex Injection. Dosage recommendations for Kantrex Injection emphasize that in patients with renal dysfunction, adequate serum levels can be achieved with a fraction of the dose suggested for patients with normal kidney function with minimal risk of ototoxicity.
- Since urinary tract infections are often accompanied by renal impairment, does that mean I shouldn't use Kantrex Injection in such conditions?
- A Not at all. With proper precautions, Kantrex Injection is an excellent drug for the treatment of urinary tract infections, especially those due to *Proteus*, *A. aerogenes* and *E. coli*, even when renal impairment is present.
- What are the "proper precautions" in a patient with impaired renal function?
- A The package literature covers them in detail. First, the daily dose should be reduced in such a patient. Then, if he is going to receive Kantrex Injection for 7 days or more, a pre-treatment audiogram should be done, and it should be repeated at appropriate intervals during therapy. If tinnitus or subjective hearing loss develops, or if followup audiograms show significant loss of high frequency response, Kantrex therapy should be discontinued. However, therapy for 7 days or more



is seldom required because the clinical response to Kantrex Injection is so rapid.

- Q Why do you put so much emphasis on Kantrex's "rapid action"? Every antibiotic I've heard about is supposed to be "rapid acting."
- A There is such an abundance of clinical evidence about "rapid acting" that it takes Kantrex Injection out of the "supposed-to" class. 1,2,3,7,8,9,11,15,16,19,21,22,26,29,32,33 Remember, the effectiveness of Kantrex Injection therapy can usually be appraised in 24 to 36 hours. That's definite evidence of rapid action. In fact, one group of investigators reported that "the rapidity with which bacteria are killed by this agent is reflected by the promptness of the clinical response."<sup>29</sup>
- Q Does Kantrex Injection cause blood dyscrasias?
- A In extensive clinical and toxicity studies by numerous investigators, as well as almost two years of general use, not a single instance of such toxicity has been reported.
- Q Can I administer Kantrex Injection in any other way than by the intramuscular route?
- A Yes. While it's usually given intramuscularly, other routes are practicable: intravenous, intraperitoneal, by aerosol, and as an irrigating solution. Complete instructions are included in the package insert.
- Q So you think I ought to use Kantrex Injection as my first choice antibiotic in staph and gram-negative infections?
- A Yes because all evidence to date indicates that it is bactericidal against a wide range of organisms...rapid acting...does not encourage development of bacterial resistance...is well tolerated in specified dosage...and has not caused any blood dyscrasias.

#### KANTREX CAPSULES

for local gastrointestinal therapy... not for systemic infections

- Why can't I use Kantrex Capsules for systemic medication?
- A Because there is only negligible absorption of Kantrex from the gastrointestinal tract. 3,5,6,8,28,34 Thus, capsules cannot provide effective blood levels.
- Then what are KANTREX Capsules used for?
- A Preoperative bowel sterilization, and local treatment of intestinal infections due to kanamycin-sensitive organisms.
- Q I've been using neomycin for preoperative bowel sterilization. Why should I switch to Kantrex Capsules?
- A Because Kantrex has been rated as "superior to neomycin" for this purpose. It provides rapid and satisfactory control of coliforms, clostridia, staphylococci and streptococci; yeasts do not proliferate; stool concentrations of the drug are exceptionally high; and nausea, vomiting or intestinal irritation have not been observed. 5.6
- What advantages do Kantrex Capsules offer me in the treatment of intestinal infections?
- A high degree of effectiveness against most of the pathogens responsible for such infections: Salmonella, Shigella, Staph. aureus, E. coli and Endamoeba histolytica. Moreover, their use has been "remarkably free of any side effects." <sup>81</sup>



#### INJECTION KANAMYCIN SULFATE INJECTION

#### INDICATIONS

Infections due to kanamycin-sensitive organisms, particularly staph or "gram-negatives": enito-urinary infections; skin, soft tissue and post-surgical infections; respiratory tract infections; septicemia and bacteremia; osteomyelitis and periostitis.

#### DOSAGE: INTRAMUSCULAR ROUTE

Recommended daily dose is 15 mg. per kg. of body weight, in 2 to 4 divided doses.

For intramuscular administration, KANTREX Injection should be injected deeply into the upper outer quadrant of the gluteal muscle.

When the recommended precautions are followed, the incidence of toxic reactions to KANTREX is low. In well hydrated patients under 45 years of age with normal kidney function, receiving a total dose of 20 Gm. or less of KANTREX, the risk of ototoxic reactions is negligible.

In patients with renal disease and impaired renal function, the daily dose of Kantrex should be reduced in proportion to the degree of impairment to avoid accumulation of the drug in serum and tissues, thus minimizing the possibility of ototoxicity. In such patients, if therapy is expected to last 7 days or more, audiograms should be obtained prior to and during treatment. Kantrex therapy should be stopped if tinnitus or subjective hearing loss develops, or if audiograms show significant loss of high frequency response.

#### OTHER ROUTES OF ADMINISTRATION

KANTREX should be used by intravenous infusion only when the intramuscular route is impracticable. KANTREX can also be employed for intraperitoneal use, aerosol treatment, and as an irrigating solution. See package insert for directions.

#### PRECAUTIONS

Use of antibiotics may occasionally result in overgrowth of non-sensitive organisms. If superinfection appears during therapy, appropriate measures should be taken.

Available in rubber-capped vials as a ready-to-use sterile aqueous solution in two concentrations (stable at room temperature indefinitely):

KANTREX Injection, 0.5 Gm. kanamycin (as sulfate) in 2 ml. volume. KANTREX Injection, 1.0 Gm. kanamycin (as sulfate) in 3 ml. volume.

#### CAPSULES (for local gastrointestinal therapy; not for systemic medication)

#### INDICATIONS AND DOSAGE

For preoperative bowel sterilization: 1.0 Gm. (2 capsules) every hour for 4 hours, followed by 1.0 Gm. (2 capsules) every 6 hours for 36 to 72 hours.

For intestinal injections: Adults: 3.0 to 4.0 Gm. (6 to 8 capsules) per day in divided doses for 5 to 7 days. Infants and children: 50 mg. per kg. per day in 4 to 6 divided doses for 5 to 7 days.

Preoperative use of Kantrex Capsules is contraindicated in the presence of intestinal obstruction. Although only negligible amounts of Kantrex are absorbed through intact intestinal mucosa, the possibility of increased absorption from ulcerated or denuded areas should be

KANTREX Capsules, 0.5 Gm. kanamycin (as sulfate), bottles of 20 and 100.

REFERENCES:

1. Andrieu, G., Monnier, J., and Bourse, R.: Presse Med. 67:718, 1959.

2. Berger, S. H., and Wehrle, P. F.: Ann. N. Y. Acad. Sci. 76:136, 1958.

3. Bunn, P. A., Baltch, A., and Krainyak, O.: Did. 76:109, 1958.

4. Bunn, P. A., and Baltch, A.: New Eng. J. Med. 259:859, 1958.

5. Cohn, I., Jr.: Ann. N. Y. Acad. Sci. 76:212, 1958.

6. Cohn, I., Jr.: Ann. N. Y. Acad. Sci. 76:212, 1958.

7. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Naumann, D. E.: J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Parent, Med. Sci. 76:319, 1958.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1959.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1950.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1950.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1950.

8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1950.

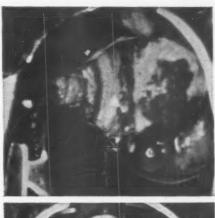
8. Cronk, G. A., and Jacobe, J. Lab. & Clin, Med. 53:838, 1950.

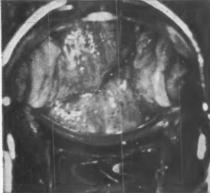
8. Cronk, G. A., and Jacobe, J. Lab. & Clin, J. Lab. & Clemo. 8:149, 1958.

8. Jacobe, J. Lab. & Clin, Jacobe, J. Lab. & Clin, J. L

Bristol

LABORATORIES INC. • Syracuse, New York





# MONILIAL VAGINITIS a common problem increasing year by year'

# MYCOSTATIN

VAGINAL specific / highly effective / safe
TABLETS CANDIDIASIS is especially serious in diabetics . . . during
pregnancy . . . in the debilitated . . . and when broad spectrum antibiotics have been
administered in high dosage, with or without concurrent administration of cortisone or

CLINICAL RESULTS. In 26 patients (11 pregnant) with vaginal moniliasis, treatment with Mycostatin Vaginal Tablets was completely successful in 92% of cases. Marked to moderate improvement was shown in the remainder.<sup>2</sup>

In a series of 59 patients with candidiasis (31 pregnant), intravaginal therapy with Mycostatin proved 100% successful in the pregnant patients; similar response was shown in 96.3% of the nonpregnant cases.<sup>3</sup>

SUPPLIED: Each Mycostatin Vaginal Tablet — individually foil wrapped contains Mycostatin, 100,000 units, and lactose, 0.93 Gm. Packages of 15 with applicator. Also available: Mycostatin Oral Tablets . . . Ointment . . . Dusting Powder . . . Powder for Suspension . . . Cream.

REFERENCES: 1. Lee, A.F., and Keifer, W.S.: Northwest Med. 53:1227 (Dec.) 1954. • 2. Caruso, L.J.: New York J. Med. 58:1688 (May 15) 1958. • 3. Pace, H.R., and Schantz, S.I.: J.A.M.A. 182:268 (Sept. 22) 1956.

SQUIBB



Squibb Quality - the Priceless Ingredient

HYCCOTATIN'S IS A SQUIBB TRADEMARK

related steroids.

December, 1959

er

ng

in

nas

a-

by

he

Page 51



# WAREXIN

IS LETHAL TO—FUNGI, BACTERIA, VIRUSES, RESISTANT SPORES—IN LESS THAN 1 HOUR—AND YET IS NON-TOXIC!



\*WAREXIN: Clorpactin® (a group of hypochlorous derivatives) to which buffers have been added for stability.

#### PREVENT CROSS-INFECTION!

Sterilize with WAREXIN

#### Can safely be used for:

- All instruments made of stainless steel or other widely used corrosion-resistant alloys — even fine stainless hypodermic needles.
- 2. Articles made of rubber, plastic, non-porous fibers, glass, porcelain, enamel.
- 3. Complex equipment such as anaesthesia apparatus, heart-lung machines, artificial kidneys, etc.
- 4. Containers such as colostomy bags, urinals, air filters.
- 5. Special surfaces: hospital and laboratory walls, floors, tables.

#### MIX WITH ORDINARY TAP WATER

Because Warexin concentrate is a true Cold Sterilizing Agent, it is unnecessary to use distilled water. Just add 1 level measure to each quart of tap water. Warexin solution gives you effective kill in 1 hour or less.

ECONOMICAL! A 5 oz. bottle makes 12-16 quarts of solution. Cost: approximately 27¢ a quart!





Lattimer, John K., and Spirito, A. L.: Clorpactin for Tuberculosis cystitis: Instrument sterilization, Journ. of Urology, Vol. 73, No. 6, June, 1955. • Wolinsky, E., Smith, M. M. and Steenken, Wm. Jr., Tuberculocidal Activity of Clorpactin. A New Chlorine Compound, Antibiotic Medicine, 1:382-384, July, 1955. • Sanders, Murray and Soret, M. G.: Virucidal activity of WCS-90, Antibiotics and Chemotherapy, Vol. V, No. 11, Nov. 1955. • Gliedman, M. L., Lt. (MC) USNR, Grant, R. N. Capt. (MC) USN, Vestal, B.L., B.S., and Karlson, K.-E., M.D.; Impromptu Bowel Cleansing and Sterilization, Surgery, 43:282-287. • From The Textbook, Extracorporeal Circulation, Edited by Dr. J. Garrott Allen, Page 87; Charles C. Thomas, Publisher.

#### NOW

...a new way
to relieve pain
and stiffness
in muscles
and joints

INDICATED IN:

MUSCLE STIFFNESS

LUMBOSACRAL STRAIN

SACROILIAC STRAIN

WHIPLASH INJURY

BURSITIS

SPRAINS

TENOSYNOVITIS

FIBROSITIS

FIBROMYOSITIS

LOW BACK PAIN

DISC SYNDROME

SPRAINED BACK

"TIGHT NECK"

TRAUMATIC STRAINS

POSTOPERATIVE

- Exhibits unusual analgesic properties, different from those
- of any other drug 

  Specific and superior in relief of SOMAtic pain
- Modifies central perception of pain without abolishing natural
- Relaxes abnormal tension of skeletal muscle defense reflexes



N-isopropyl-2-methyl-2-propyl-1, 3-propanediol dicarbamate

- More specific than salicylates Less drastic than steroids
- More effective than muscle relaxants

SOMA has an unique analgesic action. It apparently modifies central pain perception without abolishing peripheral pain reflexes. Soma is particularly effective in relieving joint pain. Patients say that they feel better and sleep better with Soma than with any previously used analgesic, sedative or relaxant drug.

Soma also relaxes muscle hypertonia, with its stresses on related joints, ligaments and skeletal structures.

ACTS FAST. Pain-relieving and relaxant effects start in 30 minutes and last 6 hours.

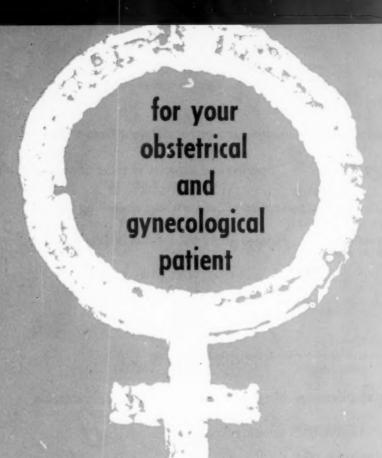
NOTABLY SAFE. Toxicity of SOMA is extremely low. No effects on liver, endocrine system, blood pressure, blood picture or urine have been reported. Some patients may become sleepy on high dosage.

EASY TO USE. Usual adult dose is one 350 mg. tablet 3 times daily and at bedtime.

SUPPLIED: Bottles of 50 white sugar-coated 350 mg. tablets. Literature and samples on request.



WALLACE LABORATORIES, NEW BRUNSWICK, N. J.



## BACULIN VAGINAL TABLETS

FUNGICIDAL ... BACTERICIDAL ... PROTOZOICIDAL COMPREHENSIVE TREATMENT OF VAGINAL INFESTATION.

A single BACULIN vaginal tablet generally destroys the causes vaginitis, namely Trichomonas Vaginalis, Candida Albicans, and non-specific organisms. Prescribe BACULIN vaginal tablets in your next case of non-venereal vaginitis.

## esplex

ACCIDENTS OF PREGNANCY CAN NOT BE CURED. THEY MUST BE PREVENTED  $\operatorname{\mathsf{des}}\nolimits plex$  is a clinically proved antiabortive.

desplex, a unique combination of ultramicronized diethylstilbestrol and vitamins C, and B complex, was shown 96% effects in carrying 1200 difficult pregnancies to term.\(^1\) For assurance of a successful pregnancy, prescribe desplex tablets. Now contains hesperidin complex.

## BANAUSEA

ANTINAUSEANT, ANTIEMETIC - BAN NAUSEA AND VOMITING OF PREGNAND . . . SAFELY . . . EFFECTIVELY . . . ECONOMICALLY.

Just prescribe BANAUSEA tablets, one upon arising and one at bedtime. Turn your patients' blue mornings pink with BANAUSEA tablets.

Samples upon request.

Reference: 1. Peña, E. F., Med. Times, 82-921, 1954.



Amfre-Grant, Inc., Brooklyn 26, N. Y.





### lifesaving technique

for the unborn





IVE

causes

bicans,

ablets in

REGNANC

e at

### includes high citrus intake

Abortion-prone mothers deliver live babies in nearly 9 out of 10 pregnancies

Reporting on 134 pregnancies in 100 habitual abortion patients, Javert\* describes a management program that resulted in live deliveries in all but 16 pregnancies. The previous 95.2 per cent rate of spontaneous abortions was reduced to 11.9 per cent by his comprehensive regimen which includes a high citrus intake (supplying up to 350 mg. of vitamin C daily), supplemented by 150 mg. of ascorbic acid and 5 mg. of vitamin K daily. Javert believes these antihemorrhagic vitamins "serve as a 'never-leak' ... keeping physiologic decidual hemorrhage from becoming pathologic."

AVERAGE CITRUS INTAKE TO SUPPLY 350 MG. VITAMIN C

28 oz. orange or grapefruit juice

1 grapefruit

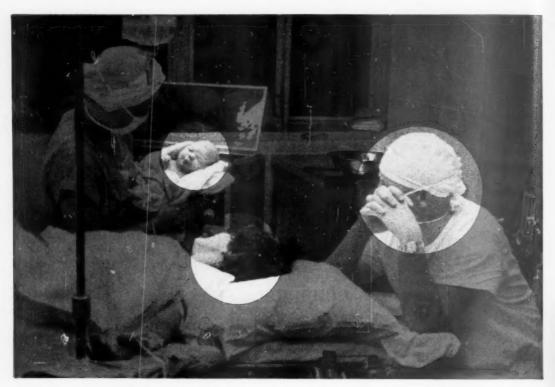
2 oranges 2 tangerines or

½ grapefruit 1 orange

16 oz. orange juice

Florida Citrus Commission Lakeland, Florida

\*Javert, C. T.: Obst. & Gynec. 3:420, 1954; Cf. Greenblatt, R. B.: Obst. & Gynec. 2:530, 1953.



With Cervilaxin, the 1st stage remaining after 3.5 cm. cervical dilatation was found to be 43% to 51% shorter than with oxytocin alone...¹

"A number of our colleagues have insisted that (oxytoein) drip alone is adequate to produce these results. Our experience has convinced them that with the combined use of (oxytocin) and Cervilaxin, the remainder of the first stage, beyond an average of about 3.5 cm. dilatation is 43% to 51% less than with (oxytocin) alone."

CERVILAXIN® the highly purified, standardized preparation of relaxin—"third hormone of pregnancy"2—is indeed "a worthwhile adjunct to the medical induction of labor . . ."<sup>3</sup>

Given by intravenous drip, alone or with oxytocin, early in spontaneous or induced labor at term, Cervilaxin acts physiologically and safely. It (1) softens the cervix, (2) eases delivery, by softening cervical and perineal tissues, and (3) avoids birth injuries, by diminishing cervical and perineal resistance to the expulsive forces of labor. In fact it makes the use of oxytocin safer as well as more efficient.

CERVILAXIN is supplied in 2-ml. vials containing 20 mg./ml., with detailed instructions for administration by intravenous drip.

References: 1. Rothman, E., Bentley, W.G., and Floyd, W.S.: Am. J. Obst. & Gynec. 78:38, 1959. 2. Stone, M.L., Sedlis, A., and Zuckerman, M.: ibid. 76:544, 1958. 3. Sands, R.X.: Canad. M.A.J. 78:935, 1958.

Products of Original Research



THE NATIONAL DRUG COMPANY

Philadelphia 44, Pa.

CE-930/59

Page 58

Am. J. Obst. & Gynec.

In a recent placebo-controlled study of 112 patients complaining of nausea and vomiting of pregnancy, Moessner<sup>1</sup> reports 94 per cent relief of symptoms with Prozine. Optimum dosage was low, side-effects notably infrequent and mild.

Prozine not only exerts a potent action upon the vomiting mechanism itself, but also controls apprehension and agitation as well as motor excitability by acting on both the hypothalamic and thalamic areas of the brain. Prozine offers effective therapy in purely psychic conditions and in psychic conditions resulting from, or contributing to, organic disease.

1. Moessner, G.F.: To be Published, Western J. Surg.

### Gravida I, Nausea and Vomiting 0





Affects the thalamic and hypothalamic areas of the brain

## PROZINE

meprobamate and promazine hydrochloride, Wyeth

SPECIFIC CONTROL THROUGH DUAL ACTION



\*Trademark

%

ne '''3 or

it ns

Y /59

ec.

Complete...for



Loromex Compact

offers you the most for your discriminating patients

Contains: Koromex Coil spring diaphragm
Koromex Jelly—regular size tube
Koromex Cream—trial size
(inclusion of jelly and cream allows
patient to select the one best suited
to physiological variants)
Koromex Introducer

\*Sanitary plastic, zippered storage bag, washable, appealingly feminine Also available with flat spring Koromex or with arcing diaphragm (Koro-Flex)

HOLLAND-RANTOS CO., INC. · 145 HUDSON STREET · NEW YORK 13, N.Y.

quick, accurate early pregnancy diagnosis...



new, 3-day oral test for pregnancy

### Pro-Duosterone®

anhydrohydroxyprogesterone 50.00 mg. activated by ethinyl estradiol 0.03 mg. per tablet

safe . . . physiologic . . . therapeutic

Pregnancy may now be diagnosed safely, simply and accurately in its earliest weeks by oral administration of Pro-Duosterone® tablets four times daily—with each meal and at bedtime—for only three consecutive days. In the nonpregnant patient uterine bleeding usually occurs 3 to 7 days after progesterone therapy.¹ No bleeding occurs when pregnancy exists; on the contrary, gestation is protected.² Moreover, in short-term functional amenorrhea regular menstrual cycles are usually restored by oral progestogen.¹

The speed and precision of this oral diagnostic test are unsurpassed, and "no laboratory equipment, animals, or specimens are needed." The 3-day, oral Pro-Duosterone test for pregnancy is also less costly than biologic methods. Finally, full diagnostic and therapeutic efficiency is assured by the small estrogen component of the Pro-Duosterone formula since "Progesterone has no action whatsoever in the absence of estrogens." Supplied: Bottles of 24 pink tablets. Roussel Corporation, 155 E. 44th St., New York 17

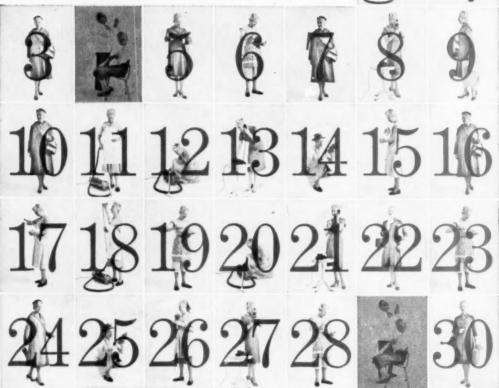
Hayden, G. E.: Am. J. Obs. & Gynec. 76:271, 1958.
 New & Nonofficial Drugs: J.A.M.A. 168:181, 1958.
 Page, E. W.: GP 9:53, 1954.

December, 1959

Page 61

only one injection today of





31

can effectively maintain a patient from the day you read this to the next issue of this journal for sustained anabolic and climacteric therapy in female and male

specify

approximately 4 weeks of effective therapy with only one injection

- minimizes or eliminates unwanted sexual effects
- well tolerated and convenient administration—low viscosity permits easy IM injection with small-gauge needle

DELADUMONE relieves physical, mental and emotional distress in the climacteric and corrects hormonal imbalance and protein loss.

Other indications: prevention of lactation

postpartum breast engorgement osteoporosis in men and women

Dosage: 1 to 2 cc. as a single intramuscular injection, every 3 to 4 weeks, depending on clinical response.

Supply: Vials of 1 and 5 cc. Each cc. contains

90 mg. testosterone enanthate and

4 mg. estradiol valerate.

for convenient, effective oral therapy

Squibb Methyltestosterone and Ethinyl Estradiol Bottles of 100 and 1000 tablets. Each tablet provides 4 mg. methyltestosterone and 0.008 mg. ethinyl estradiol.



Squibb Quality-the Priceless Ingredient

Deladumone'® and 'Dumone'® are Squibb trademarks.



but they need your help in planning their family

## Delfen

Precepting

1E MODERN CHEMICAL SPERMICIDE

THE SPERMICIDAL GEL WITH BUILT-IN BARRIER

RESCRIBED WITH CONFIDENCE FOR SIMPLE, EFFECTIVE CONTRACEPTION

### **NEW AND EXCLUSIVE**

## FOR SUSTAINED TRANQUILIZATION

MILTOWN (meprobamate) now available in 400 mg. continuous release capsules as

## Meprospan-400



JUST ONE CAPSULE LASTS ALL DAY

#### HIGHER POTENCY FOR GREATER CONVENIENCE

- relieves both mental and muscular tension without causing depression
- does not impair mental efficiency, motor control, or normal behavior

Usual dosage: One capsule at breakfast, one capsule with evening meal

Available: Meprospan-400, each blue capsule contains 400 mg. Miltown (meprobamate)

Meprospan-200, each yellow capsule contains 200 mg. Miltown (meprobamate)

Both potencies in bottles of 30.

WALLACE LABORATORIES, New Brunswick, N. J.

CHE-8427

ER

N

Now

in inflammatory anorectal disorders . . .

### The Promise of Greater Relief

the first suppository to contain

hydrocortisone for effective control of proctitis

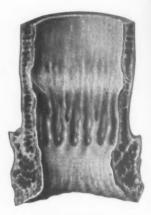
- Proctitis accompanying ulcerative colitis
- Radiation proctitis
- Postoperative scar tissue with inflammatory reaction
- Acute and chronic nonspecific proctitis
- Acute internal hemorrhoids
- Medication proctitis
- Cryptitis



**Ulcerative Colitis** 



**Radiation Proctitis** 



Postoperative Scar Tissue

Supplied: Suppositories, boxes of 12. Each suppository contains 10 mg. hydrocortisone acetate, 15 mg. extract belladonna (0.19 mg. equiv. total alkaloids), 3 mg. ephedrine sulfate, zinc oxide, boric acid, bismuth oxyiodide, bismuth subcarbonate, and balsam peru in an oleaginous base.

Wyanoids® HC

Rectal Suppositories with Hydrocortisone, Wyeth





advancing with surgery

## ETHICON®

sutures

stronger more pliable

electron beam sterilized

ETHICON

### HYPERTENSION

"When chlorothiazide is used, lower and,hence,less toxic dosages of other antihypertensive agents become effective in controlling blood pressure. Chlorothiazide does not reduce blood pressure in normotensive subjects, although the drug induces the same increase in salt excretion."

Freis, E.D.: J.A.M.A. 169:105, (Jan. 10) 1959.

Desage: One 250 mg. tablet DIURIL b.i.d. to one 500 mg. tablet DIURIL t.i.d.

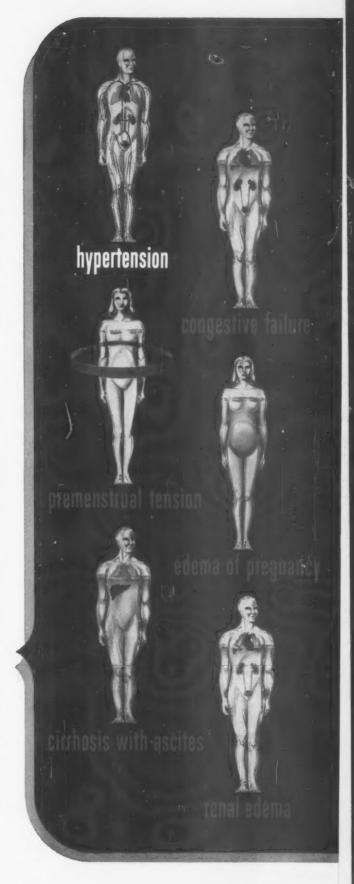
D D B CHLOROTHIAZIDE

a continuing and consistently outstanding record of safety and efficacy in:

Supplied: 250 mg. and 500 mg. scored tablets DIURIL (Chlorothiazide). DIURIL is a trademark of Merck & Co., Inc. Additional information is available to the physician on request.



©1959 Merck & Co., INC.





prevent "morning sickness" the night before...

## Bendectin

Just 2 Bendectin tablets at bedtime. In clinical trials, 1-3 this dosage schedule relieved morning sickness symptoms in more than 95% of cases.

Bendectin combines three complementary therapeutic actions: antispasmodic/antinauseant/pyridoxine supplementation to prevent this annoying discomfort.

Nulsen, R. O.: Ohio State Med. J. 53:665, 1957.
 Personal communications: 1956-57.
 Towne, J. E.: Internat. Rec. of Med. 171:584, 1958.

the weight problem in pregnancy

to

control

**TENUATE** 

THE WM. S. MERRELL COMPANY NEW YORK • CINCINNATI • ST. THOMAS, ONTARIO

TRADEMARKS : BENDECTING, "TENUATE"



before, during, and after childbirth

### **VISTARIL**...eases mental and physical discomfort

When you give her VISTARIL, confidence replaces anxiety—but not to the point of euphoria. The effectiveness of VISTARIL in pre- and postpartum nausea and vomiting adds greatly to the patient's comfort. VISTARIL enhances the action of opiates, thus decreasing narcotic requirements and lessening the possibility of respiratory depression and reduced circulatory and cortical function.

Supply: Capsules, 25 mg., 50 mg. and 100 mg.; Oral Suspension, 25 mg. per 5 cc. teaspoonful; Parenteral Solution, 10 cc. vials and 2 cc. Steraject® Cartridges-25 mg. hydroxyzine HCl per cc.

A Professional Information Booklet containing further information is available from the Medical Department on request.

Plizer Science for the world's well-beingTM

PFIZER LABORATORIES, Div., Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.

anti-



### greater antibiotic activity

Milligram for Milligram, DECLOMYCIN exhibits 2 to 4 times the activity of tetracycline against susceptible organisms. (Activity level is the basis of comparison—not quantitative blood levels—since action upon pathogens is the ultimate value.\*) Provides significantly higher serum activity level...

### with far less antibiotic intake

DECLOMYCIN demonstrates the highest ratio of prolonged activity level to daily milligram intake of any known broad-spectrum antibiotic. Reduction of antibiotic intake reduces likelihood of adverse effect on intestinal mucosa or interaction with contents.

## unrelenting peak antimicrobial attack

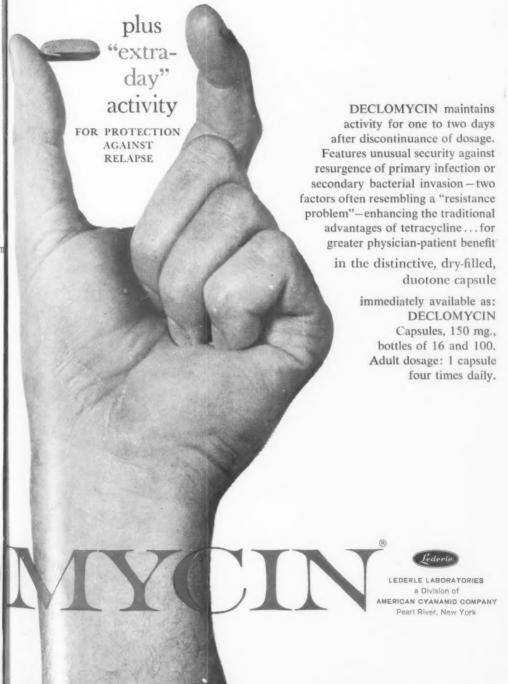
The DECLOMYCIN high activity level is uniquely constant throughout therapy. Eliminates peak-and-valley fluctuation, favoring continuous suppression. Achieved through remarkably greater stability in body fluids, resistance to degradation and a low rate of renal clearance.

\*Hirsch, H. A., and Finland, M.: New England J. Med. 260:1099 (May 28) 1959.

ECIO

Demethylchlortetracycline Lederle

## ce of antibiotic design



4 times s. tive

ake

vel ...

longed l-spectrum good of contents.

stant tion,

d, M.: I. Med. ) 1959.

### IN NAUSEA AND VOMITING OF PREGNANCY

Avoids unnecessarily diffuse or diverso drug action: effective in economical once-a-day dosage



Has no known contraindi-cations; free of hepatic, hypotensive, and hemato-logic hazards observed with phenothiazines



## PLEASE NOTE! BONINE

(FORMERLY CALLED

**BONAMINE**)

is the new name for the SAME superior product

Pfizer: Solones for the world's well-boling

### faster recovery, greater comfort for your OB-GYN patients



Administered before and after cervicovaginal surgery, irradiation, delivery, and office procedures such as cauterization, Furacin cream promptly controls infection; reduces discharge, irritation and malodor; hastens healing. Furacin cream is active in the presence of exudates, yet is nontoxic to regenerating tissue, does not induce significant bacterial resistance nor encourage monilial overgrowth.

## FURACIN° CREAM

FURACIN 0.2% in a fine cream base, water-miscible and self-emulsifying in body fluids. Tubes of 3 oz., with plastic plunger-type vaginal applicator. Also available: FURACIN Vaginal Suppositories.



THE NITROFURANS—a unique class of antimicrobials EATON LABORATORIES, NORWICH, NEW YORK

Standard preoperative procedure to control bleeding

adrenosem\*

SALICYLATE
(Brand of carbazochrome salicylate)

**OPERATING ROOM** 

Proven effective by over four years of clinical use,

millions of doses

In hemostasis blood clotting is only one factor. Restoration of capillary integrity is of primary importance. Adrenosem controls bleeding and cozing by decreasing excessive capillary permeability and promoting the retraction of severed capillary ends. 1-20

Surgical Use

Adrenosem is recommended preoperatively where bleeding presents a problem. Minimal bleeding provides a clearer operative field and facilitates operative procedures. 9-20,23 Postoperatively, it lessens the need for transfused blood. 3-6.9-11.18.16.18.20,28

#### **Medical Use**

Adrenosem is an effective hemostatic where vascular anomalies exist, such as telangiectasia, purpuras, epistaxis, and others. 1-3.6.9-11.27-29 At recommended dosage levels there are no contraindications.

Supplied: Ampuls, 1 cc., 5 mg.; Tablets, 1 and 2.5 mg.; Syrup, each 5 cc., 2.5 mg. Potency of all dosage forms is stated in terms of the active ingredient, adrenochrome monosemicarbazone.

Write for descriptive literature and dosage

\*U. S. Pat. 2581850, 2506294

THE S. E. MASSENGILL COMPANY

BRISTOL, TENNESSEE . NEW YORK . KANSAS CITY . SAN FRANCISCO

## drenosem SALICYLATE

(Brand of carbazochrome salicylate)

#### effective in more than 200 clinical disorders

Adrenosem has proved effective, both prophylactically and therapeutically, in numerous operative procedures and pathological conditions. Following is a partial list of the many indications for Adrenosem.

tonsillectomy adenoidectomy pharyngectomy mastoidectomy ectomy myoplasty septectomy turbinectomy rhinoplasty laryngectomy epic onchotomy tracheoplasty tracheostomy pneumonectomy pleurectom hy pericardiorrhaphy splenectomy stomatoplasty chelloplasty uvulectomy ophagectomy gastrectomy enterotomy proctectomy proctopexy sphincen ectomy hernioplasty wederotomy prostatectomy vulvectomy hysterector raction skin grafts soar excisions dermabrasion gastrointestinal blee axis metrorrhagia monorrhagia cervical ooze antepartum and postpart m capillary hemorrhage during hedulin, dicumerol or x-ray ther ingiectasia hemorrhagie retinitis subarachnoid hemorrhage ecchymosis

#### THE S. E. MASSENGILL COMPANY

RISTGL, TENNESSEE . NEW YORK . KANSAS CITY . SAN FRANCISCO



for thetense and nervous patient

lectomy

y epig

Ctomy

lectomy

ohincten

rector

blee

stpar

y then

osis

relief comes fast and comfortably

-does not produce autonomic side reactions

-does not impair mental efficiency, motor control, or normal behavior.

Usual Dosage: One or two 400 mg. tablets t.i.d.

Supplied: 400 mg. scored tablets, 200 mg. sugarcoated tablets or as MEPROTABS\*-400 mg. unmarked, coated tablets.

Miltow

meprobamate (Wallace)



WALLACE LABORATORIES / New Brunswick, N. J.

## DISSOLVES INTRAVASCULAICE

NOT JUST A NEW DRUG... A NEW THERAPY

## AGIASE

Fibrinolysin (Human)



1. Moser, K.M.: J.A.M.A. 767(1695 (Aug. 2) 1955

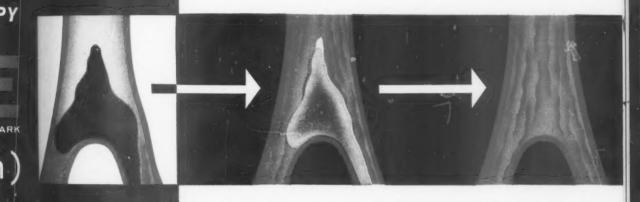
2. Cliffton, EvE .: J. Am. Geriatrics Soc. 6:118, 1984

3 Sussman B. J. and Fitch, T. S. P.: J. A. M. A. 767:1705 (Aug. 2) 18 4 Singher, H. O., and Chappie, R.V.: Clin. Med. 6.439 (March) 18

ORTHO PHARMACEUTICAL CORPORATION, RARITAN, N. J

ACLOTS

# in thrombophlebitis and pulmonary embolism



Clinically proved,<sup>1-3</sup> ACTASE has a specific lytic effect upon the venous thrombus or pulmonary embolus. Patients respond rapidly, often dramatically, to the clot-dissolving action of an intravenous infusion of this physiologic fibrinolysin.<sup>4</sup> A significant decrease in length of hospitalization following thrombophlebitis, as well as a reduction in the threat of pulmonary embolism, is now possible. In one series of patients with deep thrombo-

phlebitis, some of whom had previously suffered pulmonary emboli, no occurrence of pulmonary emboli was reported following administration of ACTASE.<sup>1</sup>

Ortho

COMPLETE INFORMATION AVAILABLE ON REQUEST.



What do you look for in a prenatal supplement, Doctor? Calcium, of course, and iron, as well as the essential vitamins and minerals. (With new Pramilets, you get: a good supplemental dosage of phosphorus-free calcium plus important iron-ferrous fumarate-plus all the other necessary nutrients.) What does your pregnant patient look for in a prenatal supplement? Convenient dosage? A tablet she can swallow? A pretty bottle for her dresser? Make it Pramilets. then. She gets them all—and you get a formula that will carry her

> New Pramilets: Comprehensive vitamin-mineral support with just one Filmtab \_ daily.

(TH) PRAMILETS - ABBOTT'S PHOSPHORUS-FREE PRENATAL SUPPLEMENT

through term. Pramilets, in grace-

ful Table Bottles

of 100 Filmtabs.

today

ron,
vitavith
t: a
ge of
plus
the
regent?
? A
lets,

sive with

10C.

December, 1959

### smoothly confidently

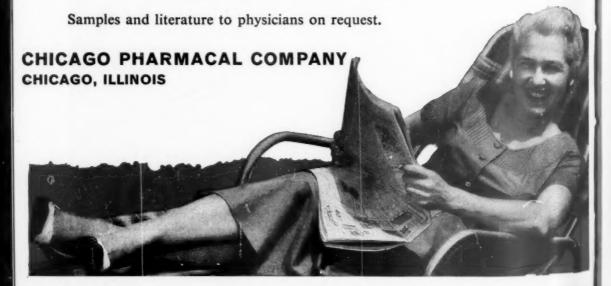
### comfortably through estrogen deficiencies

- Simple oral dosage, plus prompt relief from such common menopausal symptoms as "hot flashes," headaches, nervousness—these advantages commend ESTROSED therapy to physician and patient.
- The clinically proved benefits of ethinyl estradiol and reserpine are supplied in a single tablet...to correct estrogen imbalance...to control accompanying emotional instability.
- For safe, effective management of menopausal patients . . . for potent, well-tolerated estrogen therapy . . . for safe tranquilization . . . for convenient, economical medication, prescribe

## estrosed

Indications: hypo-ovarianism, menometrorrhagia, menopausal syndrome, postmenopausal therapy. Dosage: 1 or 2 tablets two or three times a day, according to symptoms.

Supplied: bottles of 100 and 1000 tablets. Each tablet contains Reserpine, 0.1 mg., and Ethinyl Estradiol, 0.01 mg.



### NO OTHER THYROID PRODUCT

es

end

nd

en

is used so widely and so often...stocked by so many leading pharmacies...regarded throughout the world as the pioneer in thyroid standardization and the original standard of comparison for all thyroid preparations

### ALWAYS SPECIFY ARMOUR THYROID



ARMOUR PHARMACEUTICAL COMPANY

KANKAKEE, ILLINOIS

Armour Means Protection

December, 1959

Page 85

#### FOUND: a dependable solution to

"the common st gynecole ic office problem"

ALBICANS, Haemophilus vaginalis, or cane bacteria, is still the commonest gynecologic office problem. cases of chronic or mixed infection, are often extrantial and by one or more of these pathogens, TRICOFURON IMPROVED cleared symptoms in 70; virtually all were severe, chronic infections which had persisted despite previous therapy with other agents. "Permanent cure by both laboratory and clinical criteria was achieved in 56. . . . "
Ensey, J. E.: Am. J. Com. 77:115, 1959

## TRICOFURON

Improved

- · Swiftly relieves itching, burning, malodor and leukorrhea
- Destroys Tricho nonas vaginalis, Candida (Monilia) albicans, Haemophilus vaginalis Achieves clinical and cultural cures where others fail Nonirritating and esthetically pleasing

#### 2 steps to lasting relief

- 1. POWDER for weekly insufflation in your office. MICOFUR®, brand of nifuroxime, 0.5% and FUROXONE®, brand of furazolidone, 0.1% in an acidic water-dispersible base.
- 2. SUPPOSITORIES for continued home use each morning and night the first week and each night thereafter—especially during the important menstrual days. MICOFUR 0.375% and FUROXONE 0.25% in a water-misciple base.

Rx new box of 24 suppositories with applicator for more practical and economical therapy.

NITROFURANS—a unique class of antimicrobials EATON LABORATORIES, NORWICH, NEW YORK

the true specific for monitial vaginitis

## GENTIA-JEL

CURES ARE QUICKER Gentia-jel's unsurpassed monilia-killing power results in quicker cures and less recurrence. IMMEDIATE RELIEF This soothing jel provides fast, gratifying relief of vulvar itching and burning... destroys fungi and bacteria. COMPLETE COVERAGE Gentia-jel disperses completely over vaginal and cervical mucosa, penetrates into all folds and bathes the vulvar labia.



start therapy
with GENTIA-JEL
... it works
when others fail

## GENTIA-JEL

## the true specific for monilial vaginitis

Gentian violet is the most effective agent known for the destruction of Monilia acbicans. Numerous nonstaining preparations have been used in treating vaginal moniliasis but have proven far lead effective than gentian violet.

Gentia-jel's effectiveness is proved by its rate of cures during the last trimester of pregnancy, when mycotic infections are most difficult to cure. Gentia-jel is shown to be over 3% clinically effective, and has been used succe, stulling hundreds of case, refractory to other tierapies.

Monilial reinfection is avoided with Gontia-jel by eliminating two major caucas: (1) there is no manuscrition of tablets or suppositories into the vagina and (2) applicators are sever reused, but discarded.

And, Gentia jel is easy for your patients to use. (1) Prior to retiring for the night, patients lie back with knees flexed, insert applicator and instill Gentia-jel. (2) Applicator is removed and discarded and a vaginal tampon or pledget of cotton is inserted in the introitus. A sanitary pad should be worn.

Treatment should be continued over 12 days to assure a negative smear.

Gentia-jel is supplied in packages of 12 single-dose disposable applicators.

WHY WAIT UNTIL OTHER THERAPIES FAIL...
START YOUR PATIENTS WITH GENTIA-JEL

WESTWOOD PHARMACEUTICALS.

Buffalo 13, New York



cushioned comfort—
now
two ways





The cushioned comfort and sensitivity built into both the regular RAMSES® Diaphragm and the new RAMSES BENDEX,® a bow-bend Diaphragm, contribute to the physical ease and emotional security that encourage patient cooperation.

The regular RAMSES Diaphragm, suitable for most women, is distinguished by a soft cushioned rim and flexibility in all planes to permit complete freedom of motion. The complete unit

-the new RAMSES "TUK-A-WAY"® Kit #701 with diaphragm, introducer and jelly, is attractively packaged in a new zippered case which opens top and side.

For those women who need a different type of diaphragm, the RAMSES BENDEX is now available, retaining all the desirable flexibility of RAMSES coil-spring construction. The bow-bend or arc-ing type of construction makes it especially suitable for the woman with structural abnormalities such as cystocele or rectocele. No introducer is required. Further information about the new BENDEX may be obtained from your local Schmid representative.

RAMSES Jelly,\* uniquely suited for use with either type of RAMSES Diaphragm, further contributes to the patient's comfort and protection by flowing freely over the rim and surface to lubricate the diaphragm, aid in insertion, and protect the patient for ten full hours.

When you fit your patient with one of these RAMSES Diaphragms you are providing essential inner security. She is assured she can plan her family according to her wishes, safe in the knowledge that she is using not only the most reliable method—diaphragm and jelly, which reduces the likelihood of conception by at least 98 per cent<sup>1</sup>—but the most comfortable choice—RAMSES Diaphragm and Jelly.

1. Tietze, C.: Proceedings, Third International Conference Planned Parenthood, 1953.

\*Active agent, dodecaethyleneglycol monolaurate 5%, in a base of long-lasting barrier effectiveness.

RAMSES, "TUK-A-WAY," and BENDEX are registered trade-marks of Julius Schmid, Inc.

JULIUS SCHMID, INC., 423 West 55th Street, New York 19, N. Y.

**New from Lederle** 

a logical combination in appetite control

## BAMADEX®

meprobamate eases tensions of dieting

d-amphetamine depresses appetite and elevates mood



...without insomnia

...without barbiturate hangover

Each coated tablet (pink) contains: d-amphetamine sulfate . . . 5 mg. meprobamate . . . . . 400 mg. Dosage: One tablet taken one-half to one hour before each meal.



LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

all through pregnancy ...

a cheerful outlook
without autonomic toxicity reactions

relieves
anxiety
insomnia
fretfulness
tension
headache
muscular
tension

By permission of the Cleveland Health Museum, possessors of the original

One of your safest adjuncts for successful management of pregnancy Meprobamate, Wyeth

Philadelphia 1. Pa

December, 1959

York

nec.

Page 91

# IN HEARTBURN OF PREGNANCY, PATIENTS SAY... TASTY IS THE WORD FOR 'teaspoon dose"

TITRALAC is being widely prescribed in heartburn of pregnancy, simple hyperacidity, and peptic ulcer because of these outstanding features:

- · creamy, mint flavor...no chalky taste
- · acts in seconds...lasts for hours
- non-constipating... no acid rebound

ful TITRALAC Liquid approximates 2 tablets which contain 0.36 Cm. glycine and

ACID NEUTRALIZING POWER

only I teaspoonful

ALSO WITH A SPASMOLYTIC ..



during pregnancy or lactation make sure of dietary adequacy with new low cost...

Mol-Iron Prenatal

ONLY 1 tablet daily, 1/2 the usual cost, phosphorus-free, 12 vitamins plus 10 minerals. The clinical superiority of MOL-IRON for the correction of iron deficiency during pregnancy has been established by more published reports than are available for any other iron preparation.

WHITE LABORATORIES, INC., KENILWORTH, NEW JERSEY

tic

Whites

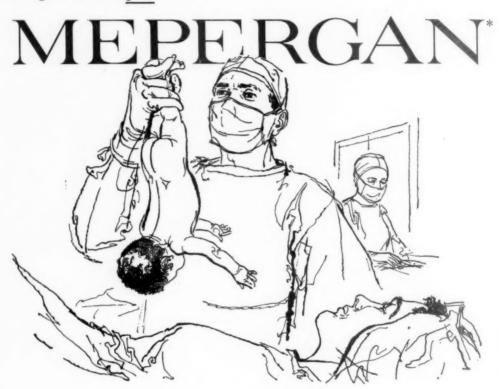
for smoother

childbirth

...and reduced risks

for infants

analgesia with a plus



With MEPERGAN as a part of management, obstetrical patients are usually relaxed, free of apprehension, and sleep quietly between their pains. Awakened easily, they are mentally alert and cooperative. Multiparae frequently report that the discomfort of labor is less than on previous occasions. Labor is often shortened. Nausea and vomiting are rare. The anesthetic course is smooth. And, most important, there is decreased hazard of hypoxia for both mother and infant. Widespread clinical experience points to MEPERGAN's 1:1 ratio of promethazine and meperidine to be most satisfactory for most patients.

See package circular for complete information on use of MEPERGAN.

\*Trademark for Promethazine Hydrochloride and Meperidine Hydrochloride, Wyeth.



# NOW many more hypertensive patients may have THE FULL BENEFITS OF CORTICOSTEROID THERAPY

Except for one case of mild blood-pressure elevation (150/90) no hypertension was seen in any of 1500 patients as a result of treatment with DECADRON—the new and, on a milligram basis, most potent of all corticosteroids. Hypertension induced by other steroids diminished or disappeared.



treats <u>more</u> patients <u>more</u> effectively Thus with DECADRON, hypertension no longer appears to be a contraindication to successful corticosteroid therapy. And the dramatic therapeutic impact of DECADRON was virtually unmarred by diabetogenic or psychic reactions... Cushingoid effects were fewer and milder... and there were no new or "peculiar" side effects. Moreover, DECADRON helped restore a "natural" sense of well-being.

tAnalysis of clinical reports

\*DECADRON is a trademark of Merck & Co., Inc. @1959 Merck & Co., Inc.



MERCK SHARP & DOHME

DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

Does more than curb appetite... also relieves the tensions of dieting



# Helps you keep your patient on your diet

AN EXTENSIVE SURVEY shows that in 68% of overweight persons there is an emotional basis for failure to limit food intake. Appetrol has been formulated to help you overcome this problem and to keep your overweight patient on your diet.

THIS NEW ANORECTIC does more than give you dextro-amphetamine to curb your patient's appetite. It also gives you Miltown to relieve the tensions of dieting which undermine her will power. IN PRESCRIBING APPETROL, you will find that your patient is relaxed and more easily managed so that she will stay on the diet you prescribe.

Usual dosage: 1 or 2 tablets one-half to 1 hour before meals.

Each tablet contains: 5 mg. dextro-amphetamine sulfate and 400 mg. Miltown (meprobamate, Wallace).

Available: Bottles of 50 pink, uncoated tablets.

1. Kotkov, B.. Group psychotherapy with the obese. Paper read before The Academy of Psychosomatic Medicine, October 1958.



WALLACE LABORATORIES, New Brunswick, N. J.

CPL-31

# Infemale urethritis age makes a difference

#### BEFORE THE MENOPAUSE,

localized urethral infection is highly prevalent but "easily overlooked" because pain and discomfort are frequently referred to other areas.<sup>1</sup>

#### FURACIN® INSERTS (formerly Furacin Urethral Suppositories)

are antibacterial...anesthetic...gently dilating...provide rapid control of both pain and infection<sup>2</sup>...0.2% Furacin and 2% diperodon•HCI (an efficient local anesthetic), in a water-dispersible base. Each hermetically sealed in silver foil, box of 12.

#### AFTER THE MENOPAUSE,

estrogen deficiency leads to atrophy of the urethral mucosa, irritation, increased susceptibility to infection...a frequent source of pelvic distress.<sup>3</sup>

#### FURESTROL® SUPPOSITORIES

are estrogenic as well as antibacterial, anesthetic and gently dilating... provide "progressive histologic normalization" and prompt symptomatic relief<sup>4</sup>... 0.2% Furacin, 2% diperodon HCl, and 0.0077% (0.1 mg.) diethylstilbestrol, in a water-dispersible base. Each hermetically sealed in orchid foil, box of 12.

REFERENCES: 1. Barrett, M. E.: J. M. Assoc. Alabama 26:144, 1956. 2. Youngblood, V. H.: J. Urol., Balt., 70:926, 1953. 3. Youngblood, V. H.; Tomlin, E. M.; Williams, J. O. and Kimmelstiel, P.: Tr. Southeast. Sect. Am. Urol. Assoc., Atlanta, Ga. (Apr. 7-11) 1957, p. 40-43. 4. Youngblood, V. H.; Tomlin, E. M. and Davis, J. B.: J. Urol., Balt., 78:150, 1957.

NITROFURANS —a unique class of antimicrobials EATON LABORATORIES, NORWICH, NEW YORK

Just one prescription for Engran Term-Pak" (270 TABLETS)



calling for one tablet a day will carry her through term to the six-week postpartum checkup. This means you are assured of a nutritionally perfect pregnancy, and she realizes major savings.





\* And when baby comes, specify Engran baby drops—full vitamin support in half the volume of most similar preparations—lasts twice as long. Supplied in 15 cc. and 50 cc. bottles. Convenient 'Flexidose' Dropper assures accurate dosage.

uterine
relaxation
without
hormonal action
for painful
menstrual cramps

new

### VASODĪLAN°

a myo-

-vascular relaxant

specifically relieves painful menstrual cramps by relaxing spasm or hypermotility through *direct action* on the myometrium

effectiveness confirmed clinically—In one study, VASODĪLAN relieved menstrual cramps in 82 per cent of the patients. Another investigator reports relief in 15 of 16 cases with acute debilitating dysmenorrhea.<sup>2</sup>

dosage-For dysmenorrhea, give 10 or 20 mg. (1 or 2 tablets) three or four times daily 24 to 72 hours prior to the expected onset of menstruation.

availability-VASODĪLAN Tablets, 10 mg., bottles of 100. VASODĪLAN Injection, Ampuls, 2 cc. (5 mg./cc.), boxes of 6.

For complete details on indications, dosage, administration and clinical background of VASODĪLAN see the brochure on this product available on request from Mead Johnson & Company, Evansville 21, Indiana.

references: (1) Voulgaris, D. M.: Dysmenorrhea—Treatment with Isoxsuprine, Obstetrics and Gynecology, to be published. (2) Krantz, K. E.: Detailed reports in Mead Johnson research files.



74118



#### both blood picture and patient respond to TRINSICON®

Investigators<sup>1,2</sup> have determined that low serum iron may be accompanied by insidious vitamin B<sub>12</sub> deficiencies which result from subnutrition, increased demand, or lack of intrinsic factor. Coexisting vitamin C deficiencies also have been found.<sup>3</sup>

These studies suggest that an anemia may be multiple in nature—that optimum results would be derived from a combination of therapeutic agents.

Trinsicon offers therapeutic quantities of all known hematinic factors. Prescribe two Pulvules® daily to provide assured response in all treatable anemias.

Trinsicon® (hematinic concentrate with intrinsic factor, Lilly)

A. M. A. Arch. Int. Med., 99:346, 1957.
 Am. J. Obst. & Gynec., 70:1309, 1955.
 Lancet, 1:448, 1957.

ELI LILLY AND COMPANY . INDIANAPOLIS 6, INDIANA, U.S.A.

### "SUNNY SIDE UP"



Specific effectiveness in morning sickness with

MORNIDINE®

### for

- Prevention of nausea and vomiting
- Selective action on the emetic center
- "Excellent" or "good" relief
- Little or no drowsiness

Mornidine (brand of pipamazine), another achievement of Searle Research, provides selective action on the vomiting center with very little drowsiness. Mornidine is extremely effective in morning sickness. In 145 pregnant patients, 91 per cent had "excellent" or "good" relief from nausea and vomiting.

Doses of 5 mg. at intervals of six to eight hours provide effective relief all day. Suggestion: first tablet to be taken upon awakening.

For patients unable to retain oral medication when first seen, Mornidine may be administered intramuscularly in doses of 5 mg. (1 cc.).

G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.



## To control nausea and vomiting of pregnancy ...to relieve accompan ing g.i. discomfort

Investigators report that 'Combid' Spansule capsules:

- control nausea and vomiting of pregnancy all day and all night with just one dose q12h
- reduce spasm and hypersecretion and thus relieve accompanying L. heartburn, distention and discomfort
- allay anxiety and tension often seen with nausea and vomiting 3. of pregnancy

Each 'Combid' Spansule capsule contains:

- the anticholinergic Darbid® (brand of isopropamide), 5 mg.
- the tranquilizer-antiemetic Compazine® (brand of prochlorperazine), 10 mg.

b.i.d.

Combid Spansule



#### Concomitant measure: as a prophylaxis

NYLMERATE Solution Concentrate as a vaginal douche

- · Therapeutic (Bactericidal and tricho-
- Acidic (4.1 pH in dilution)
   Reaches innermost recesses via low surface tension
- Use . . . twice daily (1 capfull to 2 quarts water)
- Economical

iec.

Available only on your prescription (Eliminates possibility of excessive or unwarranted vaginal douching)

Specify pint bottles with measuring cap (Nyimerate: A brand of phenylmercuric acetate)



Check these important features of NYLMERATE

- · Positive Trichomonacidal and Monilicidal action
- Symbiotic organisms eradicated by its bactericidal potency
- · Low surface tension allows for deep epithelial cell penetration
- Re-establishes normal vaginal flora and prevents recurrences
- Simple to use... morning and night applications, including treatment during menstrual period



Prescribe: "Nylmerate Jelly with applicator" 3 oz. and 5 oz. tubes



#### EFFECTIVE AND WELL TOLERATED

#### in depression

NIAMID has been found to be strikingly effective and well tolerated in a broad range of depressive states including a wide variety of the milder depressive syndromes, as well as the masked depression so frequently seen in general practice. These syndromes include: depression associated with the menopause. postoperative depressive states and senile depression; depression accompanying chronic or incurable illness, such as gastrointestinal and cardiovascular disorders and inoperable cancer.

#### in angina pectoris

NIAMID, in intensive clinical tests, has proved to have a high degree of safety and to be a valuable adjunct in the management of the anginal syndrome. NIAMID produces striking symptomatic improvement in angina patientsmarkedly reduces the pain, severity and frequency of anginal episodes, reduces nitroglycerin requirements, and provides an increased sense of well-being. Since dramatic improvement is seen in some patients, it is wise to advise the patient against overexertion - his disorder still holds potential dangers despite relief of symptoms.

DOSAGE: Start with 75 mg. daily in single or divided doses. After a week or more, adjust the dosage, depending upon patient response, in steps of one or one-half 25 mg. tablet. Once improvement is seen, gradually reduce dosage to the maintenance level. Many patients respond to NIAMID within a few days, others in 7 to 14 days. A few patients may require as much as 200 mg, daily over a longer period of time before significant improvement is seen.

PRECAUTIONS: Side effects are infrequent and mild, and often lessened or eliminated by a reduction in dosage. Hypotensive effects have rarely been noted and no jaundice or other evidence of liver damage has been reported in patients receiving NIAMID. However, in patients with a history of liver disease, the possibility of hepatic reactions should be kept in mind.

SUPPLY: NIAMID is available as 25 mg. (pink) and 100 mg. (orange) scored tablets.

Already clinically proved in several thousand patients-

Complete references and a Professional Information Booklet giving detailed information on NIAMID are available on request.



Pfizer Science for the world's well-being

\*Trademark for brand of nialamide

PFIZER LABORATOR'ES, Division, Chas. Pfizer & Co., Inc., Brooklyn 6 New York

**5** 

a broad pressive general nopause, ompanyvascular

f safety ndrome, tients – reduces g. Since patient te relief

or more, lf 25 mg. nce level. s. A few ne before

jaundice NIAMID. atic reac-

l tablets.

ed infor-

nialamide



IN REFRACTORY CONSTIPATION IN REFRACTORY CONSTIPATION IN REFRACTORY CONSTIPATION
IN REFRACTORY CONSTIPATION IN REFRACTORY CONSTIPAT IN REFRACTORY CONSTITUTE IN REFRACTORY CONSTIPATION IN REFRACTORY CONSTIPATION

Sendal to Concentrate of Total active Principles of TABLETS/GRANULES

REHABILITATES THE
CONSTIPATED PATIENT—
HELPS RESTORE NORMAL BOWEL TONE,
RHYTHM, AND SENSITIVITY.

SUPPLIED: TABLETS: Small and easy to swallow, in bottles of 100.

GRANULES: Cocoa-flavored, in 8 and 4 ounce canisters.

The Purdue Frederick Company DEDICATED TO PHYSICIAN AND PATIENT SINCE 1892
\*Copyright 1959, The Purdue Frederick Company
\*Copyright 1959, The Purdue Frederick Company

# The Nutrient Value of LOW-PRICED CUTS of Meat

It is a common misconception that the higher-priced cuts of meat are "more nourishing" than the lower-priced cuts.

The fact is that all lean meats—beef, veal, lamb, and pork—supply approximately the same quantity of high efficiency protein, as well as a significant complement of B vitamins and essential minerals. One low-priced meat, lean pork, exceeds all other high protein foods in its content of thiamine.

Each of the low-priced cuts of lean meat listed below is approximately equivalent to the most expensive cuts of lean meat in content of protein, B vitamins, and minerals such as iron, potassium and phosphorus.

#### BEEF

Steaks: chuck, shoulder, flank, round, rump.

Pot roasts: chuck ribs, cross arm clod, round, rump.

Stews: neck, plate, brisket, flank, shank, heel of round.

#### LAMB, PORK AND VEAL

Chops, roasts, pot roasts and stews made from shoulder, breast, and shank meat.

Dishes prepared with these low-priced cuts of meat are among the most delectable. Furthermore, meat, because of its outstanding nutritional value, is an ideal food to recommend in high protein diets in both health and disease without burdening the food dollar.

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

American Meat Institute
Main Office, Chicago... Members Throughout the United States

RIO

iec.



# An Atlas of Standard Proven Operative Techniques

### **GYNECOLOGIC SURGERY and UROLOGY**

1957

547 pages

81/2" x 11"

illustrated with 161 full-page plates by DAISY STILWELL

Price,

\$2000

#### by THOMAS L. BALL, M.D.

Assistant Professor of Clinical Obstetrics and Gynecology, Cornell University Medical College; Associate Attending Obstetrician and Gynecologist, The New York Hospital, New York. With Foreword by R. GORDON DOUGLAS, M.D., Professor of Obstetrics and Gynecology, Cornell University Medical College; Obstetrician and Gynecologist-in-Chief, The New York Hospital, New York.

Incorporating the best features of atlas-type and encyclopedic reference books, GYNECOLOGIC SURGERY AND UROLOGY is a superbly written and instructively illustrated summarization of present-day thinking on surgical gynecology and female urology. Adopting the regional surgery school of thought as an advance from the long-accepted organ specialty, this is an authoritative presentation of all the significant theoretical and practical information essential for the gynecologist, urologist, pathologist, obstetrician and general surgeon.

Written by a man who has been in the forefront in this field as a teacher, investigator and clinician, this volume is truly a major contribution to gynecologic surgery literature. Reflecting the accumulated studies and experiences of Dr. Thomas L. Ball and his colleagues at The New York Hospital—Cornell Medical Center, this reference, written on the post-graduate level, embodies all the most acceptable modern theories and successful techniques of urological and bowel surgery associated with the female genitalia.

Over 568 drawings, many of them step-by-step illustrations of operative procedures, strikingly reinforce the instructive text matter and make this reference one of the most detailed illustrative volumes available on gynecologic surgery.

Embodying the essential teachings of Dr. Thomas Ball and the gynecological staff of the Department of Obstetrics and Gynecology of The New York Hospital-Cornell Medical Center, this volume is a source unequalled for:

- Successful proven surgical procedures of the entire pelvic area written on the post-graduate level.
- 2. An informative discussion of fluid balance and anesthesia.
- 3. A detailed explanation of pre-operative and post-operative care.
- A significant discussion of radiology and isotopes—material found exclusively in this book.
- 5. A complete description of all the exenteration operations.
- 6. Effective advice on psychosomatic aspects of gynecologic surgery and psychiatric evaluation of the infertile female.
- A well-organized summarization of cystoscopic studies in female cancer.

Whether you're an experienced gynecologist or a beginning resident, this significant reference can broaden your concepts of gynecology and acquaint you with the newer concepts and techniques of gynecologic surgery.

At Your Favorite Bookstore or Order on 10-Day Approval from

### The C. V. MOSBY Company

3207 Washington Boulevard, St. Louis 3, Missouri



"a new and nearly ideal skin drape...

skin adherent to the incisional edge."

Apply over operative area then

INCISE RIGHT THROUGH FILM

A new aid to aseptic surgery...

### WI-DRAPE Surgical Film

...completely isolates the patient's skin from the wound and maintains the sterility of the operative site. Skin draping by this method eliminates the use of cumbersome cloth skin towels and towel clips. Nothing used during the operation can touch uncovered skin.

A soft, sterilizable, pliant plastic, Vi-DRAPE Film is adhered to the surgically prepared skin with sterile Vi-HESIVE® Surgical Adherant and the incision made right through the transparent film. The adhered film clings closely to wound edges throughout the procedure and is impermeable to bacteria and fluids. Applicable to all contours, Vi-DRAPE Film offers extra advantages in achieving asepsis in previously difficult-to-drape areas.

Use of Vi-DRAPE Film fits easily into established routines of the surgical team. For literature and technic-for-use, write to:

AEROPLAST CORPORATION 420 Dellrose Ave., Dayton 3, Ohio.

Vi-Drape Film and Vi-Hesive Adherant are available through your surgical supply dealer. In Canada, through Fisher and Burpe Ltd.
Patents Pending

1. Adams, Ralph, M. D.: Med. Times, 86:1119-1127 (Sept.) 1958.

Initial clinical studies on Vi-DRAPE Film were conducted by Carl Walter, M.D., Peter Bent Brigham Hospital, Boston.

and for post-op use

AEROPLAST®

Spray-on Surgical Dressing

In Kraurosis and Leukoplakia Vulvae, Pruritis Vulvae et Ani, Postmenopausal and Senile Vaginitis...

### HIST-A-CORT-E

CREME

pH 4.7

ACID MANTLE HYDROCORTISONE ESTRONE PYRILAMINE MALEATE SYNTHETIC VITAMIN A



Stops itching instantly and completely.

Corrects thickening of skin-eliminates scaling.

Restores skin to normal softness and pliability.

Tends to negate necessity for surgery in Kraurosis and Leukoplakia Vulvae.

Supply: With 1/2 % hydrocortisone in 1/2 oz. and 1 oz. tubes

With 1% hydrocortisone in 1/2 oz. tubes

Sig: Apply twice daily Samples and literature on request

INCORPURATEU

IN EKCLUSIVE

ACID MANTLE

VEHICLE



THE MOST TRUSTED NAME IN DERMATOLOGICALS



DOME CHEMICALS INC.

125 West End Avenue, New York 23



When abnormal cellular metabolism accompanies stress conditions

Hesperidin, Hesperidin
Methyl Chalcone, or Lemon
Bioflavonoid Complex are
prescribed as therapeutic
adjuncts for control of
abnormal cellular activity,
and capillary and vascular
damage associated with
many stress conditions.

These stress conditions may be caused by nutritional deficiencies, environment, drugs, chemicals, toxins, virus or infection.

SUNKIST AND EXCHANGE BRAND Lemon Bioflavonoid Complex and Hesperidins are available to the medical profession in specialty formulations developed by leading pharmaceutical manufacturers.

#### Sunkist Growers

PRODUCTS SALES DEPARTMENT PHARMACEUTICAL DIVISION Ontario, California

# Maintenance of Capillary Integrity

Incidence of impaired capillary function is more frequent than previously recognized. Many publications indicate the frequency of increased capillary weakness ranges from 16% to as high as 80% of patients examined (1-4).

Reports show older people have a high incidence of capillary fragility (6). In a group of 111 patients, capillary weakness was noted to be greatest in the fifth and sixth decades (5).

Hypertensives (7, 8, 9) and those with chronic diseases such as arteriosclerosis, diabetes and rheumatoid arthritis, have shown varying degrees of capillary involvement. Hemorrhagic conditions of the brain and heart have shown localized injury in the capillary (10, 11).

Capillary fragility has been shown to be associated with many bacterial, viral and inflammatory diseases (12-23).

Various bioflavonoid materials have been evaluated for their effect upon the capillary. Degree of fragility has been determined by numerous procedures (24-30).

The therapeutic rationale of combining Hesperidin or other citrus bioflavonoids with ascorbic acid or other therapeutic agents is based on the premise that capillary weakness may be a contributing factor to the disease state and that capillary integrity should be maintained. Citrus bioflavonoids in conjunction with ascorbic acid appear to enhance the efficacy of other therapy, and help control such factors as infection, stress and nutritional deficiency even in cases not showing capillary weakness.

NOTE: For bibliography (B-701) write Sunkist Growers, Pharmaceutical Division, 720 E. Sunkist Street, Ontario, California.



You give food and friendship with every \$1 package you send to the world's hungry thru the CARE Food Crusade, New York





Because women during pregnancy are particularly prone to secondary fungal infection, they benefit from the extra

protection of nystatin.

Cosa-Tetracyn® (glucosamine-potentiated tetracycline) provides peak levels of antibiotic activity against a broad range of susceptible organisms.

Nystatin provides specific protection against overgrowth of Candida albicans.

COSA-TETRASTATIN provides tetracycline effectiveness with minimum risk of moniliasis. Supplied: Capsules (pink & black) 250 mg. Cosa-Tetracyn plus 250,000 u. nystatin

Oral Suspension (orange-pineapple flavor), 2 oz. bottle, each tsp. (5 cc.) contains 125 mg. Cosa-Tetracyn plus 125,000 u. nystatin

A Professional Information Booklet providing complete details on Cosa-Tetrastatin is available on request.

Pfizer Science for the world's well-being"

PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc. Brooklyn 6, N. Y. with your support

RETARDED CHILDREN CAN BE HELPED



#### for therapy of overweight patients

· d-amphetamine depresses appetite and elevates mood

meprobamate

eases tensions of dieting (yet without overstimulation, insomnia, or barbiturate hangover.)



#### is a logical combination in appetite control

Each coated tablet (pink) contains: meprobamate, 400 mg.; d-amphetamine sulfate, 5 mg. Dosage: One tablet one-half to one hour before each meal.



LEDERLE LABORATORIES

A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

#### ACTA ENDOCRINOLOGICA

The Official Journal of the Endocrinological Societies in Denmark, Finland, Germany, Holland, Norway, Sweden and Switzerland.

#### Vol. XXXII, Fasc. 2 CONTENTS

#### October 1959

Martay, F., et Gautheron, D.: Effets comparés de la corticotrophine et de l'adrénaline sur la glycolyse et la respiration de l'utérus de rat
Schätzle, W.: Befunde am Genitaltraktus der Ratte nach Corticotropin-Injektion und ihre Deutung unter Berücksichtigung des Zellbildes der Adenohypophyse
Hökfelt, B., and Luft, R.: The effect of suprasellar tumours on the regulation of adrenocor-
tical function  Taylor, W.: The metabolism of 21-hydroxy-5β-pregnane-3,20-dione by rabbit liver homogenate
Diczfalusy, E., and v. Münstermann, AM.: Isolation and identification of 16-oxo-oestradiol- 17β in human placentae
Teller, W., and Staib, W.: Studies on the 'differential' hydrolysis of steroid conjugates in urine. Paper chromatographic and colorimetric determinations of the main urinary
steroids following different methods of hydrolysis and extraction
Bruinsma, A. H., and de Waard, F.: Oestrogenic activity at menopausal age in women with diabetes mellitus ('diabètes gras')
Jores, J., und Kracht, J.: Wirkung von Sulfonylharnstoffverbindungen auf die Mitosenfrequenz der insulären B-Zellen
Dirscherl, W., und Glasmacher, H.: tber die lokale Wirkung von Dihydrotachysterin (AT 10)
auf das Knochengewebe der RatteGrönroos, M., and Kauppila, O.: Hormonal-cyclic changes in rats under normal conditions
and under stress as revealed by vaginal smears after Shorr staining  Brown P. S.: Urinary gonadotrophins in normal men
Boseila, AW. A., Moltke, E., and Thorsee, H.: Influence of D-thyroxine and L-thyroxine on
the basophil count in human blood
critical review

One number issued monthly, four numbers forming a volume. Three volumes yearly, the price of each volume is 50.00 Danish crowns, or \$7.25, or sh. 52/-, post free.

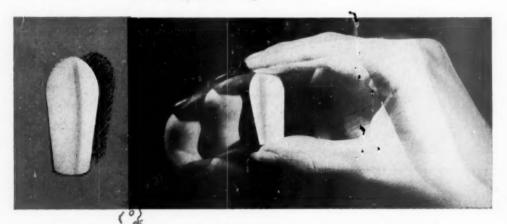
The supplements are supplied free of charge to subscribers.

Publisher: PERIODICA, 8A Boeslundevej, Copenhagen Brh., Denmark.

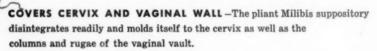
# Against the "Vaginitis Spectrum"

TRICHOMONAS MONILIA BACTERIA

A welcome clinical advance... effective medication in an appealing form



Soft and pliant as tampon, the Milibis vaginal suppository offers proved therapeutic action\* in a vehicle giving unusual clinical advantages to both patients and physician.



SHORT DOSAGE SCHEDULE-The short course of treatment with Milibis-only 10 suppositories in most cases-together with the clean, odorless, non-staining qualities eliminates psychic barriers which often interrupt longer treatments before complete cure.



SUPPLIED: BOXES OF 10

MILIBIS® Vaginal Suppositories

Now supplied with plastic applicator

SANITARY

INSURES CORRECT SUPPOSITORY PLACEMENT

\*97 per cent effective in a study of 564 cases; 94 per cent effective in a series of 510 cases.

Millbis (brand of glycobiarsol), trademark reg. U.S. Pat. Off.

# To simplify and assist PRENATAL Management

FOSFREE

Recommended Dosage: 4 Tablets Per Day

Soluble Phosphorous Free Calcium, High Pyridoxine, Vitamin B-12, Ferrous Gluconate plus Catalyst.

Samples upon Request

Pregnancy brings problems. Fosfree tablets aid in the management, prevention, and control of:

- NAUSEA
- · ANEMIA
- **© LEG CRAMPS**
- VITAMIN AND MINERAL DEFICIENCY





25 Years Successful Use Ulithout a Diaphragm

SINCE 1934
WHITTAKER LABORATORIES, Inc.
PEEKSKILL, NEW YORK,

a logical combination for appetite suppression

meprobamate plus d-amphetamine

- ... suppresses appetite ... elevates mood ... reduces tension ... without insomnia,
- overstimulation, or barbiturate hangover.



Each coated tablet (pink) contains: meprobamate, 400 mg.; d-amphetamine sulfate, 5 mg. Dosage: One tablet one-half to one hour before each meal.



LEDERLE LABORATORIES

A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

iec.

### EVER NEED HELP QUICKLY WITH A PUZZLING CASE?

For Sound, Clinical Advice on Gynecologic Problems Use This Concise, Up-to-Date Synopsis in Convenient Pocket Size



New 5th Edition

### Crossen-Beacham-Beacham SYNOPSIS OF GYNECOLOGY

Completely revised, rearranged and rewritten from a fresh point of view, the new 5th edition of SYNOPSIS OF GYNECOLOGY can provide you with up-to-date, clinical help on virtually all of your gynecologic problems. Dr. Robert Crossen and the new co-authors Drs. Daniel Beacham and Woodward Beacham present brief, succinct discussions of the anatomy, physiology, embryology, pathology, examination and diagnosis of the female reproductive system that will be extremely valuable to you in diagnosis and treatment.

The only synopsis on this subject available today, this ready reference gives you all the details of outpatient therapy for gynecologic diseases, as well as sound surgical principles. Two new chapters have been added to this revision—one on "Endometriosis" and the other on "Complications of Pregnancy." Included in the latter are new discussions of abortion and hydatidiform mole and choriocarcinoma. Twelve chapters have been completely rewritten and the others have been revised and brought up to date.

You will also find this revision includes timely discussions of such recent advances as chromosomal sex determination and abnormal hormonal production in the evaluation of intersexuality; incompetent cervix as a cause of abortion; use of oral progestogens in dysfunctional uterine bleeding, abortion and endometriosis; use of adrenal corticoids in pelvic infections and malformations associated with adrenal hyperplasia; and the use of radioactive isotopes and chemotherapeutic agents in the therapy of malignant diseases.

By ROBERT JAMES CROSSEN, M.D., Associate Professor of Clinical Gynecology and Obstetrics, Washington University School of Medicine; DANIEL WINSTON BEACHAM, M.D., Assistant Professor of Clinical Obstetrics and Gynecology, Tulane University School of Medicine; and WOODARD DAVIS BEACHAM, M.D., Professor of Clinical Obstetrics and Gynecology, Tulane University School of Medicine. Published September, 1959. 5th edition, 340 pages, 4 7/8" x 7 5/8", 106 Illustrations, including 1 two-page color insert. Price, \$6.50.

Order on 10 Day Approval from

> The C.V. MOSBY Company

THE C. V. MOSBY COMPANY 3207 Washington Blvd., St. Louis 3, Mo.	
Dear Sir:	
Please send me on 10 day approval a copy of Crossen-Beach OF QYNECOLOGY, priced at \$6.50. I understand that is satisfied, I oan return the book within 10 days with not remittance is enclosed, publisher pays the mailing charge.	f I am not completel
Payment enclosed	
(Same Return Privileges)	Open a new account for me M.D
	for me
(Same Return Privileges) Address	for me

logical prescription overweight patients

meprobamate plus d-amphetamine

...depresses appetite ... elevates mood ... eases tensions of dieting ... without overstimulation, insomnia, or barbiturate hangover.

nt of can your thors

suclogy,

that

referlogic have

er on disorna.

have

such rmal etent func-

renal

with emo-

M.D., Med-

Gyne-edition, Price,

SIS

unt

D.

ynec.



LEDERLE LABORATORIES

A Division of AMERICAN CYANAMID COMPANY, Pearl River, N.Y.





hospital use.

the gentle laxative



December, 1959

Correlates the pathological changes in the ovary with the endocrine disorders which accompany them

Morris and Scully

# OF THE OVARY

For the gynecologist, the pediatrician, the internist, the pathologist or the endocrinologist seeking to correlate and understand the pathological changes found in the ovary with the endocrine disorders which accompany them, the new Morris and Scully book, ENDOCRINE PATHOLOGY OF THE OVARY offers the only completely current and significantly essential information available on the subject. Covering the modern aspects of the problem, this presentation includes not only much previously unreported case material, but a number of new approaches to existing concepts as well.

The authors lead you through introductory chapters on modern concepts of the cells of the gonads, their embryology, sexual differentiation, sex hormone production, hormone assays, and a brief classification of various endocrine syndromes. Current thinking on non-neoplastic and neoplastic abnormalities of the ovary which are associated with endocrine effect are discussed in detail. Significant case histories of functioning tumors and related disorders observed at Massachusetts General Hospital, Peter Bent Brigham Hospital, the New England Deaconess Hospital, the Boston City Hospital, Free Hospital for Women in Brookline and Yale Medical Center are included.

By JOHN McLEAN MORRIS, M.D., Associate Professor of Gynecology, Yale University School of Medicine; and ROBERT E. SCULLY, M.D., Clinical Associate in Pathology, Harvard Medical School, Associate Pathologist, Massachusetts General Hospital, Boston.

Just published, 151 arges, 63/4" x 93/4", 75 illustrations. Price, \$8.50



The C.V. MOSBY Company

3207 Washington Boulevard, St. Louis 3, Missouri

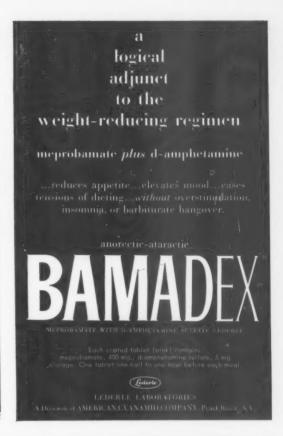
#### Changing Your Address?

#### When you move, please-

- Notify us to change your address allow us six weeks to make the change.
- (2) Mention the name of this Journal. (We publish twelve periodicals.)
- (3) Give us your old address. If possible, return the addressed portion of the envelope in which we sent your last copy.
- (4) Give us your new address—complete
  —including the Postal zone number.
- (5) Please print your name and address.

#### Thank You!

Circulation Department, The C. V. Mosby Company, Publishers, 3207 Washington Blvd., St. Louis 3, Mo.



#### SPECIALIZED SERVICES

7 DAYS

A WEEK

to Laboratories all over

North America

"The Bulletin of Laboratory Medicine" is published monthly by Biochemical Procedures to keep physicians and laboratorians abreast of current developments in the clinical laboratory field. Write for a complete set.

#### TOXICOLOGY & MISCELLANEOUS CHEMISTRIES

Lead • Arsenic • Transaminase Lipids • Antistreptolysin Hemoglobin Identification Proteins by Electrophoresis Serum Iron.• Iron Binding Capacity • Paternity Tests Copper • Magnesium

#### **ENDOCRINE ASSAYS**

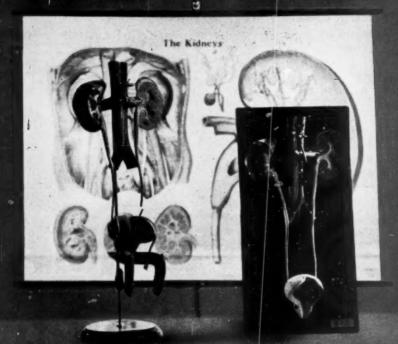
Aldosterone • Catecholamines Serotonin • 17-Ketosteroids and Fractionations • Protein-Bound Iodine • Estrogens Butanol Extractable Iodine Pregnanediol • Pregnanetriol Corticosteroids • Gonadotropins

### Please write for Fee Schedule & Mailing Containers BIOCHEMICAL PROCEDURES

12020 Chandler Boulevard North Hollywood, California

"The Laboratory for Laboratories"





History on though courters fol Clay-Adon's Lor. New York

# 6,800,000

courses of treatment\* and <u>still</u> negligible development of bacterial resistance with

# FURADANTIN

in genitourinary tract infections

\*CONSERVATIVE ESTIMATE BASED ON THE CLINICAL USE OF FURADANTIN TABLETS AND ORAL SUSPENSION SINCE 1953.

"The future of antimicrobial therapy may well rest with antibacterial chemicals more than with antibiotics."

# FURADANTIN

brand of nitrofurantoin

"...may be unique as a wide-spectrum antimicrobial agent that...does not invoke resistant mutants." 2

SENSITIVE STRAINS: PREREQUISITE TO SUCCESSFUL THERAPY

#### OVER-ALL RESPONSE OF GRAM-NEGATIVE BACTERIA TO ANTIMICROBIAL DRUGSS

	No. organisms tested	No.	sensitive (%)		oderately tant (%)		resistant (%)
Nitrofurantoin	1730	1074	(62.1%)		-	656	(37.9%)
Tetracycline	2879	1000	(34.7%)	434	(15.1%)	1445	(50.2%)
Chloramphenicol	2879	1268	(44.0%)	725	(25.2%)	886	(30.8%)
Streptomycin	2879	943	(32.8%)	368	(12.8%)	1568	(54.4%)
Sulfisoxazole	1730	452	(26.1%)		-	1278	(73.9%)

"In order of decreasing effectiveness, the activity of the drugs against gram-negative organisms was as follows: nitrofurantoin, chloramphenicol, tetracycline, streptomycin, and sulfisoxazole."

#### OVER-ALL RESPONSE OF GRAM-POSITIVE BACTERIA TO ANTIMICROBIAL DRUGS3

	No. organisms tested	No.	sensitive (%)		noderately stant (%)		resistant (%)
Nitrofurantoin	320	289	(90.3%)		_	31	(9.7%)
Penicillin	2353	515	(21.9%)	303	(12.9%)	1535	(65.2%)
Erythromycin	2853	1633	(69.4%)	308	(13.1%)	412	(17.5%)
Tetracycline	2353	987	(41.9%)	673	(28.6%)	693	(29.5%)
Chloramphenicol	1939	1593	(82.2%)	242	(12.5%)	104	(5.3%)
Sulfisoxazole	303	25	(8.3%)		-	278	(91.7%)

"For the gram-positive organisms, the order of decreasing effectiveness was: nitrofurantoin, chloramphenicol, erythromycin, tetracycline, penicillin, and sulfisoxazole, although relatively few strains were tested against the first and last drugs."

Available as Tablets, 50 and 100 mg.; Oral Suspension, 25 mg. per 5 cc. tsp.

References: 1. Seneca, H., and Lattimer, J. K.: A.M.A. Arch. Path. 64:481, 1957. 2. Waisbren, B. A., and Crowley, W.: A.M.A. Arch. Int. M. 95:653, 1955. 3. Metzger, W. I.: Antibiotics Annual 1958-1959, edited by H. Welch and F. Marti-Ibanez, New York, Medical Encyclopedia, Inc., 1959, pp. 966-971.

NITROYURANS—a unique class of antimicrobials—neither antibiotics nor sulfonamides EATON LABORATORIES, NORWICH, NEW YORK

### in childbirth...

'Thorazine' as adjunctive therapy has three advantages

### 1. helps you establish optimum levels of analgesia

In labor, 'Thorazine' reduces the tension and anxiety which intensify pain, without affecting natural uterine contractions. With 'Thorazine' therapy, the patient in labor is calm, cooperative and responds to pain only mildly.

#### 2. minimizes risk of respiratory depression

During delivery, because of Thorazine's potentiating effect, the amount of analgesic agents needed is greatly reduced. Thus, the risk of respiratory depression is minimized for both the mother and the infant.

#### 3. controls nausea and vomiting

In all three stages of childbirth, with 'Thorazine' the incidence of nausea and vomiting is markedly reduced.

#### THORAZINE\*

chlorpromazine, S.K.F.

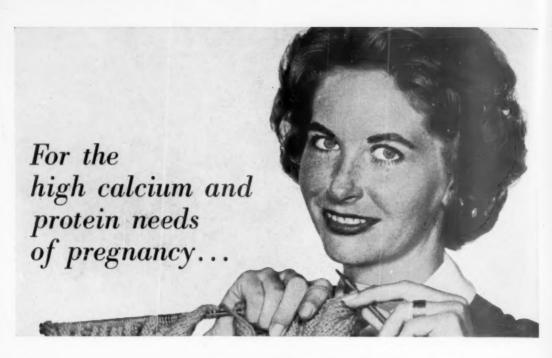
one of the fundamental drugs in medicine

#### Smith Kline & French Laboratories

\*T.M. Reg. U.S. Pat. Off.







#### New self-enriched Carnation Instant

25% more protein, calcium, B-vitamins, richer flavor than ordinary nonfat milk

New Carnation Instant can give your patients a more delicious nonfat milk—extra-rich in natural milk calcium, protein and B-vitamins. This new fresh flavor crystal-form nonfat milk can be self-enriched. The patient simply adds one extra spoonful of crystals per 8-oz. glass when mixing—to gain 25% more calcium, protein and B-vitamins than ordinary nonfat

milk—and far richer flavor. Convenience and low cost also encourage acceptance. Calorie count remains low (400 per quart), facilitating weight control.

In examining the chart, physicians will recognize the particular value of the increase in natural milk calcium, more effectively utilized than most medicinal calcium salts.

	Calcium	Protein	Riboflavin	Thiamine
National Research Council Recommended Daily Dietary Allowances During Second Half of Pregnancy	1.5 Grams	78.0 Grams	2.0 Mg.	1.3 Mg.
Amount and Percent of Daily Dietary Allowances Provided by 1 Quart of 25% self-enriched Carnation Instant	1.48 Grams (98%)	41.3 Grams (53%)	2.26 Mg. (113%)	.40 Mg. (30%)

#### 25% self-enriched Carnation Instant

Simply add 1 tablespoon extra Carnation Instant per glass, or 1/3 cup extra Carnation Instant per guart, over regular package directions.





the

The liona and pregi

FILI

AUT abso

LEDER

#### the decorative jar makes a therapeutic difference

The FILIBON jar is a handsome and handy reminder for everyday prenatal nutriional support. You can be sure she will be reminded of her FILIBON-a-day... and that the up-to-the-minute formula covers nutritional defenses throughout oregnancy.

FILIBON provides ferrous fumarate, an iron well-tolerated by even the most easily upset patients. Each small, dry-filled capsule also includes vitamin K and AUTRINIC® Intrinsic Factor Concentrate that enhances, never inhibits, B<sub>12</sub> absorption. For complete formula see Physicians' Desk Reference, page 688.

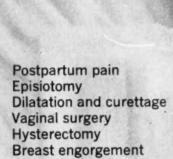
LEDERLE LABORATORIES, a Division of AMERICAN CYANAMID COMPANY, Pearl River, N. Y.





Phosphorus-free FILIBON® Prenatal Capsules Lederle

to relieve pain in OB-GYN practice...



Postspinal cephalalgia

# remember Z

# Zactirin

Ethoheptazine Citrate with Acetylsalicylic Acid. Wyeth

After using Zactirin in 92 obstetrical and postsurgical gynecological patients, Roden and Haugen¹ conclude from the patients' own reports: In obstetrical patients—"an effective analgesic for the usual types of pain occurring during the postpartum period." In gynecological patients—"satisfactorily relieves mild or moderate post-operative pain occurring as the result of major and minor surgical procedures." Side-effects—"infrequent and mild and did not necessitate discontinuing use."

Supplied: Tablets, bottles of 48. Each tablet contains 75 mg. of ethoheptazine citrate and 325 mg. (5 grains) of acetylsalicylic acid.

- 1. Roden, J.S., and Haugen, H.M.: Missouri Med. 55:128 (Feb.) 1958.
- original Wyeth non-narcotic analgesic plus anti-inflammatory action
- · orally administered
- prompt, long action—relief equivalent to that of codeine



Philadelphia 1, Pa.

#### INDEX TO ADVERTISERS

Please mention "The American Journal of Obstetrics and Gynecology" when writing to advertisers—it identifies you

Abbott Laboratories 37, 82, 83	Merck Sharp & Dohme Fourth Cover
Acta Endocrinologica 115	Merrell Company, The Wm. S 70
Aeroplast Corporation 110	Mission Pharmacal Co 117
American Meat Institute 107	
Amfre-Grant, Inc 56	National Drug Company, The 33, 58
Armour Pharmaceutical Company 85	
Arnar-Stone Laboratories, Inc 109	Organon, Inc 5
	Ortho Pharmaceutical Corporation
Biochemical Procedures 121	43, 64, 80, 81
Bristol Laboratories, Inc	Description Division Char Description
17, 18, 45, 46, 47, 48, 49, 50	Pfizer Laboratories, Division, Chas. Pfizer & Co 36, 71, 74, 75, 104, 105, 114
Carnation Company & Subsidiaries 126	Purdue Frederick Company, The 106
Chicago Pharmacal Company 84	Riker Laboratories Third Cover
Ciba Pharmaceutical Products 22, 23	Roche Laboratories, Division of Hoff- mann-La Roche Inc 24, 25
Davol Rubber Company 52, 53	Roche Laboratories, Division of Hoff-
Desitin Chemical Company 16	mann-La Roche Inc Second Cover
Dome Chemicals Inc 111	Roerig and Company, J. B 20, 21
	Rorer, Inc., William H 32
Eaton Laboratories 30, 31, 76, 86, 97, 122, 123	Roussel Corporation 61
Eaton Laboratories 30, 31, 76, 86, 97, 122, 123 Ethicon, Inc 67, 68	Roussel Corporation61 Schenlabs Pharmaceuticals, Inc92
30, 31, 76, 86, 97, 122, 123	
30, 31, 76, 86, 97, 122, 123	Schenlabs Pharmaceuticals, Inc 92
	Schenlabs Pharmaceuticals, Inc.       92         Schmid, Inc., Julius       89         Searle & Co., G. D.       9, 11, 101         Smith Kline & French Laboratories
30, 31, 76, 86, 97, 122, 123 Ethicon, Inc. 67, 68 Florida Citrus Commission 57	Schenlabs Pharmaceuticals, Inc.       92         Schmid, Inc., Julius       89         Searle & Co., G. D.       9, 11, 101
30, 31, 76, 86, 97, 122, 123 Ethicon, Inc. 67, 68 Florida Citrus Commission 57	Schenlabs Pharmaceuticals, Inc. 92 Schmid, Inc., Julius 89 Searle & Co., G. D. 9, 11, 101 Smith Kline & French Laboratories 3, 38, 39, 102, 124, 125
20, 31, 76, 86, 97, 122, 123 Ethicon, Inc. 67, 68 Florida Citrus Commission 57 Geigy Pharmaceuticals 19	Schenlabs Pharmaceuticals, Inc 92 Schmid, Inc., Julius 89 Searle & Co., G. D 9, 11, 101 Smith Kline & French Laboratories 3, 38, 39, 102, 124, 125 Squibb & Sons, E. R 26, 34, 51, 62, 63, 98
30, 31, 76, 86, 97, 122, 123 Ethicon, Inc. 67, 68 Florida Citrus Commission 57 Geigy Pharmaceuticals 19 Holland-Rantos Co., Inc. 60, 103	Schenlabs Pharmaceuticals, Inc. 92 Schmid, Inc., Julius 99 Searle & Co., G. D. 9, 11, 101 Smith Kline & French Laboratories 91 Squibb & Sons, E. R. 26, 34, 51, 62, 63, 98 Sunkist Growers 112, 113
### 200 Pharmaceuticals ### 20	Schenlabs Pharmaceuticals, Inc.       92         Schmid, Inc., Julius       89         Searle & Co., G. D.       9, 11, 101         Smith Kline & French Laboratories       3, 38, 39, 102, 124, 125         Squibb & Sons, E. R.       26, 34, 51, 62, 63, 98         Sunkist Growers       112, 113         Travenol Laboratories, Inc.       44
Ethicon, Inc	Schenlabs Pharmaceuticals, Inc. 92 Schmid, Inc., Julius 89 Searle & Co., G. D. 9, 11, 101 Smith Kline & French Laboratories 3, 38, 39, 102, 124, 125 Squibb & Sons, E. R. 26, 34, 51, 62, 63, 98 Sunkist Growers 112, 113 Travenol Laboratories, Inc. 44 Walker Laboratories, Inc. 130 Wallace Laboratories 10, 14, 54, 55, 65, 79, 96 Warner-Chilcott Laboratories 7, 119
### 200 Pharmaceuticals ### 20	Schenlabs Pharmaceuticals, Inc. 92 Schmid, Inc., Julius 89 Searle & Co., G. D. 9, 11, 101 Smith Kline & French Laboratories 3, 38, 39, 102, 124, 125 Squibb & Sons, E. R. 26, 34, 51, 62, 63, 98 Sunkist Growers 112, 113 Travenol Laboratories, Inc. 44 Walker Laboratories, Inc. 130 Wallace Laboratories 129, 41, 54, 55, 65, 79, 96
Ethicon, Inc	Schenlabs Pharmaceuticals, Inc. 92 Schmid, Inc., Julius 89 Searle & Co., G. D. 9, 11, 101 Smith Kline & French Laboratories 3, 38, 39, 102, 124, 125 Squibb & Sons, E. R. 26, 34, 51, 62, 63, 98 Sunkist Growers 112, 113 Travenol Laboratories, Inc. 44 Walker Laboratories, Inc. 130 Wallace Laboratories 10, 14, 54, 55, 65, 79, 96 Warner-Chilcott Laboratories 7, 119
Ethicon, Inc	Schenlabs Pharmaceuticals, Inc.       92         Schmid, Inc., Julius       89         Searle & Co., G. D.       9, 11, 101         Smith Kline & French Laboratories
Ethicon, Inc	Schenlabs Pharmaceuticals, Inc.       92         Schmid, Inc., Julius       89         Searle & Co., G. D.       9, 11, 101         Smith Kline & French Laboratories       12, 125         Squibb & Sons, E. R.       26, 34, 51, 62, 63, 98         Sunkist Growers       112, 113         Travenol Laboratories, Inc.       44         Walker Laboratories, Inc.       130         Wallace Laboratories       7, 179         Warner-Chilcott Laboratories       7, 119         Westwood Pharmaceuticals       87, 88         White Laboratories, Inc.       13, 14, 15, 93

While every precaution is taken to insure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index.

### for normal, healthy, comfortable pregnancies



PHOSPHORUS-FREE, HIGH-POTENCY DRY-FILL CAPSULES WITH "BUILT-IN" ANTIANEMIA FACTORS NOW WITH FLAVINGE CAPSULES

Walker LABORATORIES, INC., MOUNT VERNON, N.Y., U.S.A.

### Established Standard Therapy in Hypertension\*

Rauwiloid

#### \*Because

Rauwiloid provides effective Rauwolfia action virtually free from side effects...the smooth therapeutic efficacy of Rauwiloid is associated with significantly less toxicity than reserpine... and with a lower incidence of depression. Tolerance does not develop.

Rauwiloid is initial therapy for every hypertensive patient. ... Dosage adjustment is never a problem...

When more potent drugs are needed, prescribe one of the convenient single-tablet combinations

#### Rauwiloid® + Veriloid®

#### Rauwiloid + Hexamethonium

alseroxylon 1 mg, and hexamethonium chloride dihydrate 250 mg.

Many patients with severe hypertension can be maintained on Rauwiloid alone after desired blood pressure levels are reached with combination medication.

just two tablets

mec.

at bedtime

tablet

After full effect



# ANOTHER STUDY CONFIRMS: **EXCELLENT OBSTETRIC ANALGESIA**WITH LERITINE

Clinical results with LERITINE in 155 obstetric patients.

- rapid relief of pain: "onset of action is rapid," with "almost immediate analgesia and sedation" and "an analgesic potency 2½ times that of meperidine..."
- wide margin of safety: "respiratory depression or alteration in blood pressure was not observed . . . nausea and vomiting during labor were extremely rare . . ."
- minimal effect on newborns: "condition of the infant at the time of delivery... when compared with a group sedated with meperidine... shows a consistently higher rating."
- high patient acceptance: "We were able to obtain good to excellent amnesia in 64-66% of mothers and subjective satisfaction with the method in 83-85% of cases."

 Wizenberg, M. J., et al.: Am. J. Obst. & Gynec. 78: 405 (Aug.) 1959.

effective even for parenterally or orally as on request.

Additional literature on LERITINE is available to physicians on request.

WARNING: LERITINE may be habit-forming. Subject to Federal Narcotic Law.

\*LERITINE is a trademark of Merck & Co., Inc.



Merck Sharp & Dohme, division of MERCK & CO., INC., PHILADELPHIA 1, PA.

cy

in ng

he ith

0

to

ec-\* Gidine)

PA.